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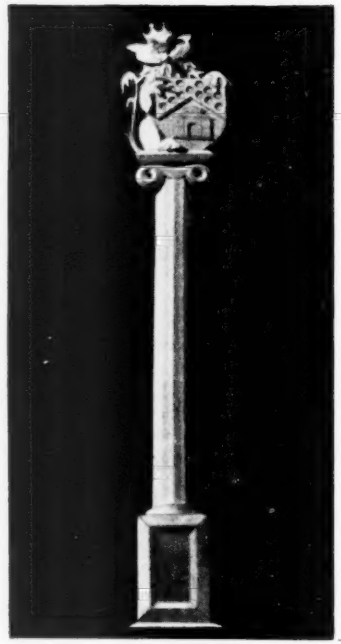

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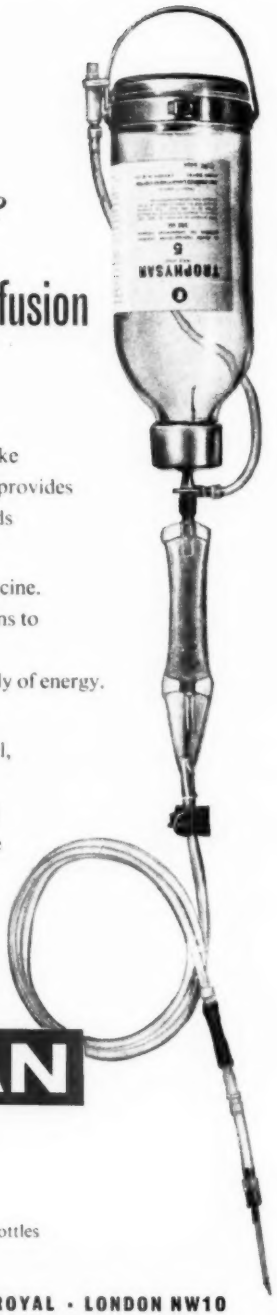

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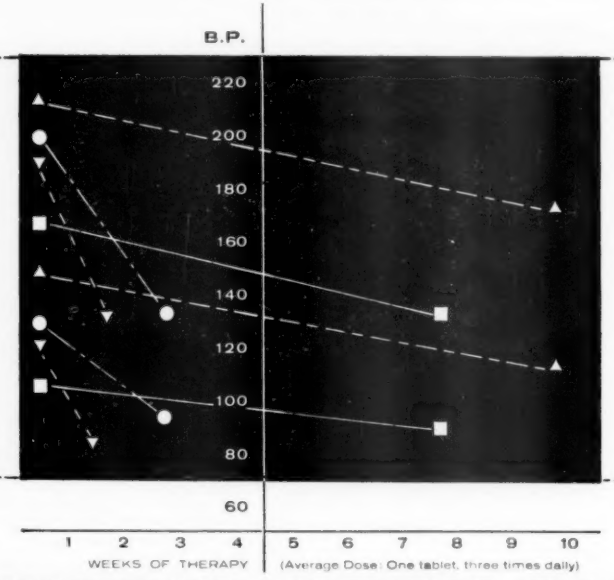

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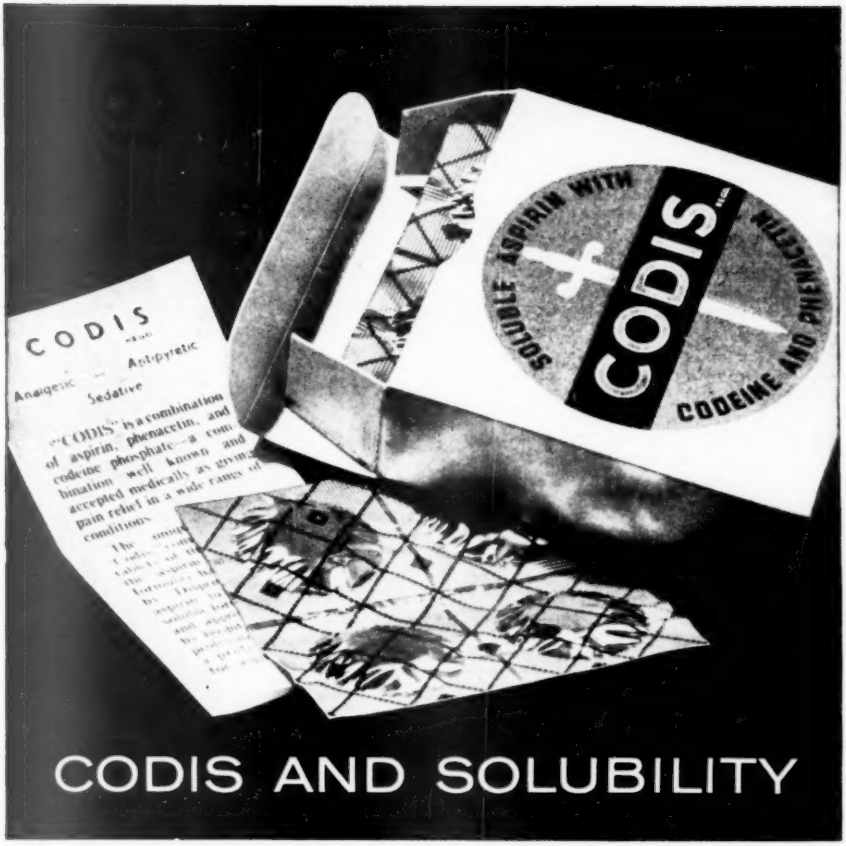

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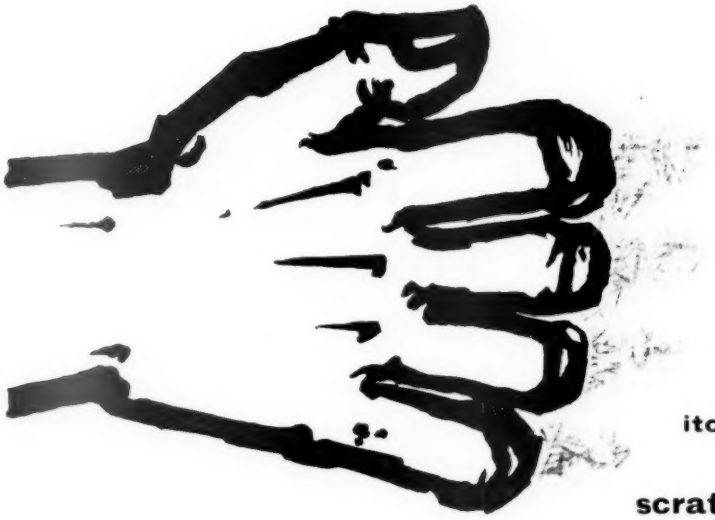

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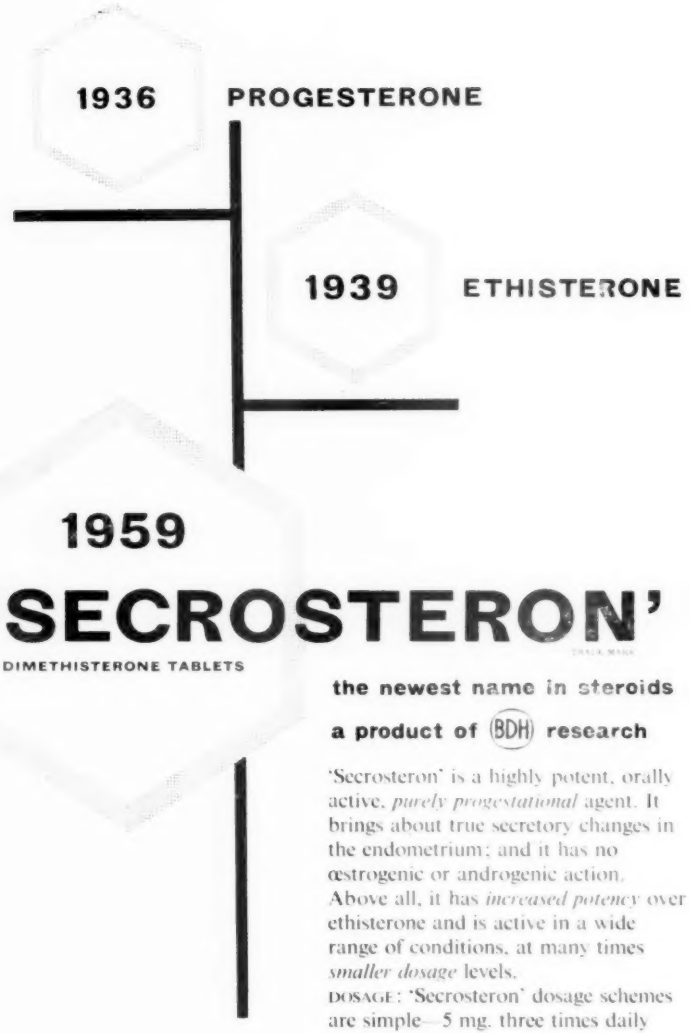

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Section of Neurology

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Meeting
April 2, 1959

DISCUSSION ON SOME CURRENT VIEWS ON SPINAL INJURIES

Dr. Jean Bénassy (Paris) read a paper dealing with (*a*) the prognosis of traumatic lesions of the cord in connexion with its blood supply, (*b*) hyperextension injuries of the cervical column, and (*c*) the problem of osteopathies in paraplegia.

Dr. J. B. Cook (Wakefield):

The Relationship of Spinal Cord Damage to Cervical Spinal Injury

For a number of years it has been accepted that traumatic quadriplegia may occur without apparent injury to the cervical spine. Such an occurrence still seems to be regarded as a mystery in spite of much having been written concerning most aspects of the problem and in spite of very little doubt as to the mechanism of damage to the spinal cord remaining. Few people see a sufficient number of recent injuries to the cervical cord to be able to correlate the cervical cord injury, the nature of the accident and the radiographic changes. When a number of such injuries are studied, however, it is possible to show that in most instances the spinal cord injury is not understood because of quite simple factors. At a spinal injuries unit, accepting patients with traumatic quadriplegia from a wide area and a variety of sources, 50% were referred without the injury to the spine having been identified.

The identification of the exact spinal injury is seldom of paramount importance if it is always realized that a traumatic quadriplegia must be associated with some sort of injury to the neck and possibly one which could be made worse by improper management. Unfortunately, the lack of radiographic evidence of spinal fracture or dislocation is sometimes taken as an indication that no particular care is necessary. A more difficult and more important problem arises when spinal cord damage is incomplete and the injury to the spine can be inferred only from the nature of the accident and a few symptoms and signs. The patient may very well present with a mild head injury which causes no anxiety and the abnormal physical signs may not appear significant to a person who has no neurological training. Because a head injury has been accepted as being the only lesion, even complete quadriplegia may be disregarded. A man of 60 tumbled and hit his forehead on the ground. He was immediately paralysed in all four limbs. He was taken to hospital and sent home. He remained at home for several days, still paralysed, developed pneumonia and was then admitted to hospital. A radiograph of the chest happened to show a gross injury to the cervical spine. Fig. 1, taken later, shows the extent of the injury.

The most frequent reason for the mechanism of cervical cord injury being obscure is faulty radiographic technique. Figs. 2 and 3 show how even a gross fracture dislocation may be missed because the site is obscured by the shadows of the shoulders. The blame must not be put on the radiographer, because the solution lies in applying traction to the head with counter-traction to the arms and it is not within the province of a radiographer to manipulate a suspected fracture of the cervical spine. The manœuvre is, however, simple and safe and should be carried out by the doctor who should accompany the patient. It may be necessary to apply a strong and steady pull with one person at the head and one on each arm.

The failure to find a gross spinal fracture because radiography has been inadequate is a problem with a simple solution and one which should not arise. It is more important to suspect an injury to the neck where the accident does not seem to be of a grave nature and it is essential to be aware of the sort of accident liable to produce cord damage.

The circumstances of an accident may appear to be commonplace and trivial to the extent of seeming silly and thereby severe spinal cord damage may not be suspected. One man sustained a quadriplegia having fallen forward when passing his water in his own garden. His friends assumed that he was in an alcoholic stupor and left him to sleep it off. Another sustained a similar injury by tripping over a mat in his bedroom. His wife could not believe that anything serious had happened and let him spend the rest of the night on the bedroom floor. It is particularly the person with marked cervical spondylosis who is liable to sustain severe cord damage from an apparently trivial injury. These examples of serious damage to the cord serve as a warning that cord injury should be suspected whenever there has been an injury to the front of the head and they indicate how misleading the story of an accident may be. It is frightening to think that a broken neck may be so easily sustained and a wonder that it does not happen more often.

FIG. 1.—Radiograph showing a healed fracture of the cervical spine in a man who had a complete quadriplegia but in whom no fracture had been suspected.

FIG. 2.—Radiograph of the cervical spine of a quadriplegic patient showing no injury.

FIG. 3.—Radiograph of the same cervical spine as in Fig. 2, showing a gross dislocation.

FIG. 4.—Radiograph of the cervical spine of a patient who sustained a traumatic quadriplegia. There is advanced cervical spondylosis and a fragment of bone detached from C.3.

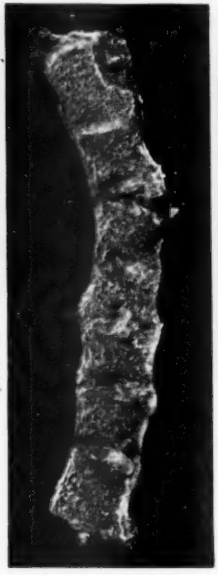

FIG. 6.—Sagittal section of the cervical spine showing traumatic rupture of the anterior longitudinal ligament extending through the intervertebral disc.

FIG. 7.—Radiograph of the cervical spine of a patient who complained of increasing spasticity in the legs. There is a detached fragment of bone lying anteriorly between C.5 and C.6.

FIG. 5.—Radiograph of the cervical spine of a patient who had a traumatic quadriplegia. There is well-marked localized intervertebral disc damage between C.3 and C.4 and at post-mortem there was a well-defined ridge of tissue at this level.

Motor-cycle and motor-car accidents, as is to be expected, are liable to cause gross injuries to the cervical spine. In these accidents mistakes may be made when there is an obvious fracture dislocation of the thoraco-lumbar region and a less obvious injury to the neck.

Some sports are liable to produce traumatic quadriplegia. It is generally accepted that diving into shallow water is especially liable to produce this sort of injury, but it is a great mistake to believe that the water must be shallow. All of four cervical cord diving injuries were sustained in water six feet or more in depth. The fractures were all comminuted ones and the patients have made little or no recovery. Rugby football is another sport which is associated with injury to the cervical spine. Two such injuries have been seen and one was the result of a collapse of the scrum. In the other it is not clear what happened. The punch on the head delivered outside a public house can hardly be described as sporting but it may cause quadriplegia. It is of interest that although such an ill-directed and unskilled punch may cause this sort of injury, quadriplegia does not occur in professional boxing. There are probably two factors to account for this difference. The quadriplegia from a casual set-to is usually in a man of middle age who has pre-existing cervical spondylosis and who is not expecting the blow. The professional boxer is a young man who must, all the time, hold his head to ride an expected blow.

There is an association between cervical spondylosis and trauma to the cervical spinal cord. The injury is usually the result of a blow on the front of the head but it need not be a forceful one. The patient is middle aged or elderly and radiographs of the cervical spine show gross intervertebral disc damage with osteophytosis. A number of the radiographs show a detached osteophyte (Fig. 4) which suggests that the anterior longitudinal ligament has been ruptured and the cervical spine allowed to extend violently but to return to its normal position. The pre-existing spondylosis probably predisposes to this sort of injury by making the neck more rigid than normal.

Payne and Spillane (1957) have demonstrated that in hyperextension of the neck ridges appear over the intervertebral discs and bulging of the ligamentum flavum may further constrict the already limited spinal canal. Fig. 5 shows advanced cervical spondylosis and at autopsy there was a pronounced bar of tissue over the most severely affected intervertebral disc space.

There remains a small group of patients who do not have cervical spondylosis and in whom adequate radiography does not wholly explain the mechanism of the cord damage. The sagittal section of the spine (Fig. 6) shows clearly how injury to the spinal cord may occur by rupture of the anterior longitudinal ligament and splitting of the intervertebral disc and this mechanism has been reported by several observers.

On routine radiography of the cervical spine, a small chip or osteophyte detached from the anterior part of the lower border of the body of the vertebra is occasionally found and causes little comment. However, the presence of such a chip is so frequently seen in association with a known extension injury to the cervical spine as to suggest that its appearance on any radiographs may be of considerable significance. Fig. 7 is a radiograph of a patient who had an increasing disability of gait due to spasticity in the legs. On being questioned he remembered that three years previously he had been riding prone on a conveyor belt when his head had struck a bar and his neck had been violently extended. He was wearing a helmet and sustained no head injury. The significance here seems to be quite definite, and whenever a chip of bone like this is seen enquiry should be made about previous head injuries. From the observation of patients with spinal injury but with minimal spinal cord damage, it is clear that they may subsequently suffer increasing disability from spasticity without increase in paralysis. It is possible that some of the patients who attend a neurological clinic with slowly increasing spasticity may have sustained an injury in the past and the detached fragment of bone may be evidence of it.

There is no doubt that many patients with traumatic quadriplegia are referred to a spinal injuries unit without the mechanism of the injury having been discovered. In fact, there is seldom any mystery. In the majority, inadequate radiography has failed to reveal a gross fracture and in many a fracture has not been suspected because of the apparently trivial nature of the accident. A considerable group consists of patients with pre-existing cervical spondylosis. In a few there is no radiographic evidence of spinal injury, but it is known that the anterior longitudinal ligament may rupture allowing extreme extension of the cervical spine. The presence of a detached fragment of bone may show that there has been such a movement in the cervical spine.

The importance of determining the exact mechanism of a cervical cord injury pales before the gravity of failing to realize that an injury to the cervical cord must be associated with an injury to the neck. Unfortunately, this elementary fact may elude the understanding with tragic results.

REFERENCE

PAYNE, E. E., and SPILLANE, J. D. (1957) *Brain*, **80**, 571.

Dr. A. G. Hardy (Sheffield):

Peripheral Destructive Procedures in the Treatment of Spastic Paraplegia

The purpose of this paper is to review one of the methods of dealing with the problems of spasticity in patients suffering from paraplegia due to lesions in the spinal cord. The method concerns the use of muscle or tendon section and peripheral nerve division in various combinations. It is not altogether a new method and some of its applications have been discussed by Elkins and Wegner (1946), Guttmann (Guttmann, 1946; Guttmann and Whitteridge, 1947), Botterell and Jousse (1948), Martin and Davis (1948), Peterson (1950) and Ritchie Russell and others (Platt *et al.*, 1958) to mention but a few of the authors who have used this form of surgical treatment.

It has been in use at the Spinal Injuries Unit in Sheffield for over ten years, and the features and results in 70 cases are to be described in detail following a short review of the problem and other present methods.

There are still gaps in our knowledge of the natural history of hypertonicity in muscle in spinal cord lesions but with the collection of this type of case in special centres we are now able to report on our clinical observations in a large series of patients. Furthermore the great reduction in the incidence of complications so frequently seen in the past has enabled us to see this hypertonicity or heightened reflex activity without the added influence of other irritating mechanisms. I refer to the stimuli derived from pressure sores, distension of bladder and bowel, infections and stones in the genito-urinary tract, corns and perforating ulcers on the feet or even badly fitting appliances.

From our own and other observations it has been difficult if not impossible to correlate the occurrence, type or degree of reflex spasm and the level or nature of the spinal cord lesion except in the obvious statement that the higher the lesion the greater the chance of widespread spasticity. As far as the type of spasm is concerned there is no question that flexor and extensor spasm can occur both in partial and complete cord lesions. One or other may predominate or each may alternate with the other. In partial lesions the hypertonicity of the skeletal muscles may completely mask existing voluntary movement as has been observed in a number of our more successful cases where the relief of extreme flexor adductor contracture has been obtained.

Kuhn and Macht (1949) reviewed 27 cases of proven anatomical transection of the cord and demonstrated 18 cases with balance of flexor spasm and extensor thrust and it is interesting to note that Head (Head and Riddoch, 1917; Riddoch, 1917) observed extensor spasm in one of his cases of complete transection 290 days after injury.

Many patients relate accentuation of their muscle spasm to the weather and particularly to cold. Mood also appears occasionally to influence spasticity in those cases with partial cord lesions, although one cannot be sure that it is not the spasticity which is causing the depression.

Suffice it to say that spasticity may be reduced in severity by excluding all the simple aggravating factors, but this alone does not relieve all cases from the burden of their disability. Indeed it is quite often necessary to institute other measures of control in instances of severe reflex disturbance.

Non-surgical measures of control.—(1) *Physiotherapy.* Of all the measures that have been used in the treatment of muscle spasm, physiotherapy must surely take pride of place. Passive stretching of spastic muscles certainly reduces tension temporarily and the benefit is greatly enhanced by doing it with the patient immersed in warm water. Pool therapy is widely used in America and of course there are also some very fine pools in this country.

The patients who derive most benefit are those who have incomplete cord lesions or those who have been under treatment from a stage of spinal shock or depressed reflex activity and on whom passive therapy has been practised from the beginning. I cannot overstress this latter point or the need to put the limbs through their full range at each treatment. This applies particularly to the extensor movement at the hip (Fig. 1).

A large number of my cases have attained a fine balance of flexor and extensor muscle tone by the apparently simple method of not allowing one group to dominate the other.

FIG. 1.—Passive extension of the hip.

(2) *Relaxant drugs.* Paraplegia units are good, although not very encouraging, testing grounds for relaxant drugs. My disappointment in the practical application of this form of therapy is shared by a great many other observers. The drugs either fail to relax the spasm or produce side-effects which render them both dangerous and impractical.

I have abandoned curare in all its forms and have likewise found mephenesin and zoxazolamine (Flexin) equally ineffective.

Chloropromazine has been useful on occasions but when it is given intravenously the patient becomes drowsy and his relaxation is such that no useful activity can be performed. I do not feel that the intravenous route is a practical one for general use.

Meprobamate has sometimes appeared successful but it is difficult to assess whether subjective relief is simply the result of the sedative action of the drug or a more direct action. Oral or intramuscular phenobarbitone is also occasionally effective.

On a few occasions temporary resort has had to be given to Omnopon and pethidine and even the celebrated cocktail:

R: Morphine hydrochloride	16 mg.
Cocaine hydrochloride	10 mg.
Syrup	15 ml.
Water add	30 ml.

Dose 30 ml. in 30 ml. of brandy twice daily.

The chief advantage of the non-surgical measures of control lies in the fact that spasticity may undergo spontaneous remission and that perseverance in passive exercise and pool therapy rather than reliance on relaxant drugs may achieve a fair measure of success.

Destructive procedures.—Destructive measures must be considered when spasticity in any of its forms progresses to a stage when pain or discomfort or interference with compensatory independence or nursing care becomes more and more a dominant feature in spite of all prophylactic measures to the contrary. They should also be considered when severe and irregular involuntary movements prevent the healing of bed sores or are associated with the distressing phenomena of autonomic hyperreflexia well described by Guttmann and others (1947).

Surgery has been used to break the reflex arc either centrally at spinal cord level or at the periphery and there are three main procedures available each with its own particular merits. Anterior rhizotomy was well reviewed by Freeman and Heimburger in 1947; I myself have little experience of this method. Intrathecal alcohol is also a well-tried method which I have used with absolute success on 21 occasions. Muscle section and nerve division, however, has been our special interest in Sheffield for over ten years.

Quite obviously the selection for division of individual muscles or nerves has its main attractions in cases in which some degree of motor power and sensation has been retained. I have used this method also in cases of complete paralysis and it has largely superseded the other and more drastic procedures. The aim is to obtain a balance in the agonist and antagonist muscle groups and to do it before secondary contractures and joint deformities have occurred.

Clinical material.—200 cases of varying degrees of paraplegia associated with excessive reflex activity and muscle hypertonicity have been seen and examined at the Sheffield Centre in the past ten years. All have received physiotherapy. 21 have had intrathecal alcohol blocks, 70 have had peripheral destructive procedures and the remainder, mainly comprising the less severe spastic disorders, have been controlled by exercise alone.

The majority of the 70 under discussion followed trauma. Table I shows the ætiology of

TABLE I

Ætiology	Cord lesion: Complete	Partial
Trauma	25	13
Disseminated sclerosis	1	11
Cord angioma		1
Spinal metastases	2	—
Epidural abscess	4	3
Spinal arachnoiditis:		
spinal anæsthesia	2	—
tuberculous meningitis	1	1
Myelopathy. Ætiology unknown	2	3
Prolapsed disc		1
	37	33

the groups together with the degree of completeness of the spinal cord lesion as this has some bearing in the results. The two cases of metastases were due, one to Hodgkin's disease and one to a carotid body tumour and probably should not be included in the series except in so far as they derived temporary benefit for a year or so prior to death. There are really three main groups, the traumatic myelopathies, the non-traumatic myelopathies of non-progressive nature and the disseminated sclerosis group all of which were of long standing and very slowly progressive in type. As might be expected this latter group had the most severe contractures and deformities.

Functional problems.—The functional problem associated with any one cord lesion has greater significance than the ætiology of the paraplegia. The cord lesions were more or less equally divided into complete and incomplete types and in each one there were the same three functional problems (Table II). The patients were bedfast or confined to their wheelchair or ambulant to a minor degree. The passive mobility of the limbs and their associated deformities broadly corresponded to the functional disability.

TABLE II.—FUNCTIONAL PROBLEMS

Group	Cord lesion		Deformity	Limb mobility
	Complete	Incomplete		
Bedfast	10	14	Flexion and adduction	Severe contracture
Wheelchair	24	12	Flexion and adduction	Partial contracture
			Flexion and extension	Alternating spasm
Ambulant	3	7	Extension and adduction	Partial contracture

Selection of cases.—In the selection of cases suitable for surgery consideration was first given to the general state of the patient and attention to all the possible irritating mechanisms. Where a vicious cycle was present, for instance a hip sore and severe flexor spasm, it was soon clear that one could not be controlled without the other (Fig. 2). In these instances, when a stage of stalemate had been reached, it was deemed best to deal with the spasticity first. One cannot safely do plastic procedures when a limb is constantly on the move.

The traumatic cases were the easiest to deal with and steadily increasing spasticity was regarded as an indication to proceed before irreversible joint contractures and muscle shortening had occurred.

The next easiest group were those cases of all ætiologies in which the spasticity and contracture were firmly established. One was simply faced with a problem in which something had to be done. Also in this group were the most interesting of all the cases, namely those with partial lesions showing evidence of voluntary motor power in the form of an ability to move the feet or toes (Fig. 3).

Lastly there was the group of cases in which the spasticity was a hindrance to ambulation in patients whose wheelchair and bed activity was otherwise quite reasonable (Figs. 4 and 5).

Operative procedures.—It was originally thought that one could directly relate types of spastic deformity and operative procedure. It was soon found out, however, that there were too many variables and it was clearly desirable to select the operation on a basis of individual assessment. The main procedures employed are listed in Table III.

TABLE III.—PRINCIPAL PROCEDURES

Iliopsoas myotomy	30	
Hamstring tenotomies	25	
Elongation of tendo Achillis	25	
Adductor longus tenotomy	19	
Obturator neurotomy:		
deep	34	47
superficial	13	

Hip flexion and adduction are dealt with by psoas section and obturator nerve division either singly or in combination. If both are severe the procedure is a single one. If one is dominant then that is dealt with first—sometimes with relief of the other, sometimes with necessity of doing a further operation at a later date.

FIG. 2.—Hip sores and severe flexor spasm.

FIG. 3.—Severe flexor adductor spasm in a partial cord lesion.

The obturator nerve division can be done as a complete section or merely as an anterior nerve section depending on the severity of the spasm.

The hamstring tenotomies are done by open operation with individual identification and section of tendon and fascial bands. The procedure is bilateral and includes both medial and lateral hamstring groups.

The lengthening of the tendo Achillis is a simple but none the less important operation and it should be emphasized that the tendon is *lengthened* and not just sectioned.

Minor operative procedures (Table IV) have proved invaluable in correcting relatively minor but impeding spastic deformities of the feet and ankles. Again the aim has been to get maximum

TABLE IV.—MINOR PROCEDURES

Toe tenotomies	5
Lateral popliteal neurotomy	3
Femoral neurotomy	2
Sciatic neurotomy	3

FIG. 4.—Spastic plantar flexion lifting the heels out of the shoes.

FIG. 5.—Spastic plantar and dorsi-flexion of the feet in the same patient.

FIG. 6.—Post-operative appearance of a patient with a partial cord lesion after multiple destructive procedures.

efficiency by reducing the number of hindering influences.

In the course of the surgical treatment of 70 cases a number of combinations of operative procedure were required: these are listed in Table V which also shows the number of occasions on which each procedure was performed. This at first sight appears formidable and criticism may be directed at what appears to be an excessive number of times that any one patient was subjected to anæsthesia and operation. This, however, is more apparent than real and the actual number of operations required are shown in Table VI.

TABLE V.—OPERATIVE COMBINATIONS

Psoas alone	6
Psoas and obturator	10
Psoas, hamstrings and obturator	14
Extension of tendo Achillis (E.T.A.)	12
E.T.A. and obturator	6
E.T.A. and hamstrings	4
E.T.A., hamstrings and obturator	3
Obturator nerve alone	9
Obturator and hamstrings	6

TABLE VI.—OPERATIONS REQUIRED

One operation	35 cases
Two operations	22 cases
Three operations	9 cases
Four operations	4 cases

There was nothing unusual or particularly difficult about the operations themselves. There was a tendency for the formation of hæmatomas which on rare occasions delayed wound healing. Gentle passive exercises were commenced after a few days. One post-operative disturbance is, however, worthy of special mention, namely a temporary exaggeration of spasm in other muscle units and occasionally imbalance of bladder function. This was more noticeable in the disseminated sclerosis group. In my experience this exaggeration settles down after wound healing.

Results.—In order to get an assessment of the real value of this method of treatment comparison and contrast has been made of the functional state of the various disabilities before and after operation. The results were thus graded on practical functional ability (Table VII).

TABLE VII.—RESULTS: KEY TO GRADING

Grade I	—Ambulant without calipers
Grade II	—Ambulant with calipers
Grade III	—Improved comfort and wheelchair independence
Grade IV	—No functional improvement

Grade I improvement implies good walking ability without the use of calipers. These patients could manage steps and stairs with ease and more than a mile of straight walking with only the aid of a stick.

Grade II could walk with calipers over short distances, surmount steps and stairs with a little difficulty but also use a wheelchair for convenience on appropriate occasions.

Grade III could not stand or walk for any practical purpose with or without calipers but their bed and wheelchair independence was greatly enhanced as was their handling by attendants. This applied to general care as in the activities of daily living and also to attention to the excretory functions.

TABLE VIII.—RESULTS—ALL LESIONS

Original state		Final grading I	II	III	IV
Bedfast	24	5	4	15	—
Wheelchair	36	3	16	15	2
Ambulant	10	5	5	—	—

TABLE IX.—RESULTS—INCOMPLETE LESIONS

Original state		Final grading I	II	III	IV
Bedfast	14	5	2	7	—
Wheelchair	12	3	3	6	—
Ambulant	7	5	2	—	—

TABLE X.—RESULTS—COMPLETE LESIONS

Original state		Final grading I	II	III	IV
Bedfast	10	—	2	8	—
Wheelchair	24	—	13	9	2
Ambulant	3	—	3	—	—

Grade IV were those in whom there was no functional improvement.

Results—all lesions (Table VIII).—The overall results were gratifying in that all but 2 cases had some improvement and that out of 60 patients previously confined to their bed or chair 28 became ambulant and 8 of these actually walked without calipers. The 10 patients who were already ambulant before operation did not improve their grading but the ease of ambulation within their grading was substantially enhanced.

Results—incomplete lesions (Table IX).—All 14 of the 24 bedfast cases who had incomplete lesions with partial paraplegias obtained great improvement in independence and 7 of them became ambulant. One of these (Fig. 6) who had severe flexor and adductor spasm at the hips and knees, associated with severe contractures in 1955, redeveloped the muscle masses in the previously stretched and inhibited antagonists following bilateral iliopsoas section and obturator nerve division and bilateral medial and lateral hamstring tenotomies in 1956. One year later he had attained the highest grade of compensatory ability.

Apart from the obvious advantages associated with the younger age groups (Table XIII) none of the 8 patients over the age of 61 came to any harm. One of these actually walked and all the others were improved in their general physical state and ease of handling. All were able to tolerate long periods in their wheelchairs.

The most significant fact which emerges from these results concerns the partial cord lesions confined to bed by reason of their spasm, contractures and deformities. In these cases evidence of long tract continuity associated with even feeble voluntary movement of the feet has been a clear indication to proceed with peripheral surgery, sometimes with the revelation of strong purposeful voluntary movement in other muscle groups once the spasm and contracture of the antagonists had been overcome.

To turn the seemingly impossible into something of value, to make the more difficult a little easier, and to remove the hindrances from the impeded is surely an achievement well worth the price of the use of destructive surgery on these unfortunate patients.

TABLE XI.—RESULTS—BEDFAST AND WHEELCHAIR GROUP (60)

Origin	Final grading I	II	III
Trauma	5	11	13
Disseminated sclerosis	—	2	9
Miscellaneous myelopathies	3	7	8
	8	20	30

TABLE XII.—RESULTS—BEDFAST GROUP ONLY

Origin	I	II	III
Trauma	4	—	3
Disseminated sclerosis	—	—	5
Miscellaneous myelopathies	1	4	7
	5	4	15

TABLE XIII.—AGE GROUPS

16 to 30 years	23
31 to 40 years	12
41 to 50 years	17
51 to 60 years	10
Over 61	8

Results—complete lesions (Table X).—As was expected the results in the complete paraplegias did not show quite such dramatic improvement. Nevertheless all 10 of those confined to bed were mobilized to wheelchair independence and 13 out of 24 cases previously confined to their chairs became ambulant with calipers over short distances on the flat.

In the important group of patients previously confined to their bed or a wheelchair (Table XI) the best results were obtained in the traumas and miscellaneous myelopathies. The disseminated sclerosis group showed a relatively lesser degree of improvement in their grading. Only 2 out of 11 cases of this latter group became ambulant in calipers.

Of the 24 bedfast cases (Table XII) 4 out of 7 of the traumatic group and 5 out of 12 of the miscellaneous myelopathies became ambulant. Thus with the exception of the disseminated sclerosis group 50% of the cases were very substantially improved.

Acknowledgments.—My thanks are due to my orthopædic colleagues Mr. F. W. Holdsworth and Mr. J. W. Dickson for their willing co-operation and surgical assistance.

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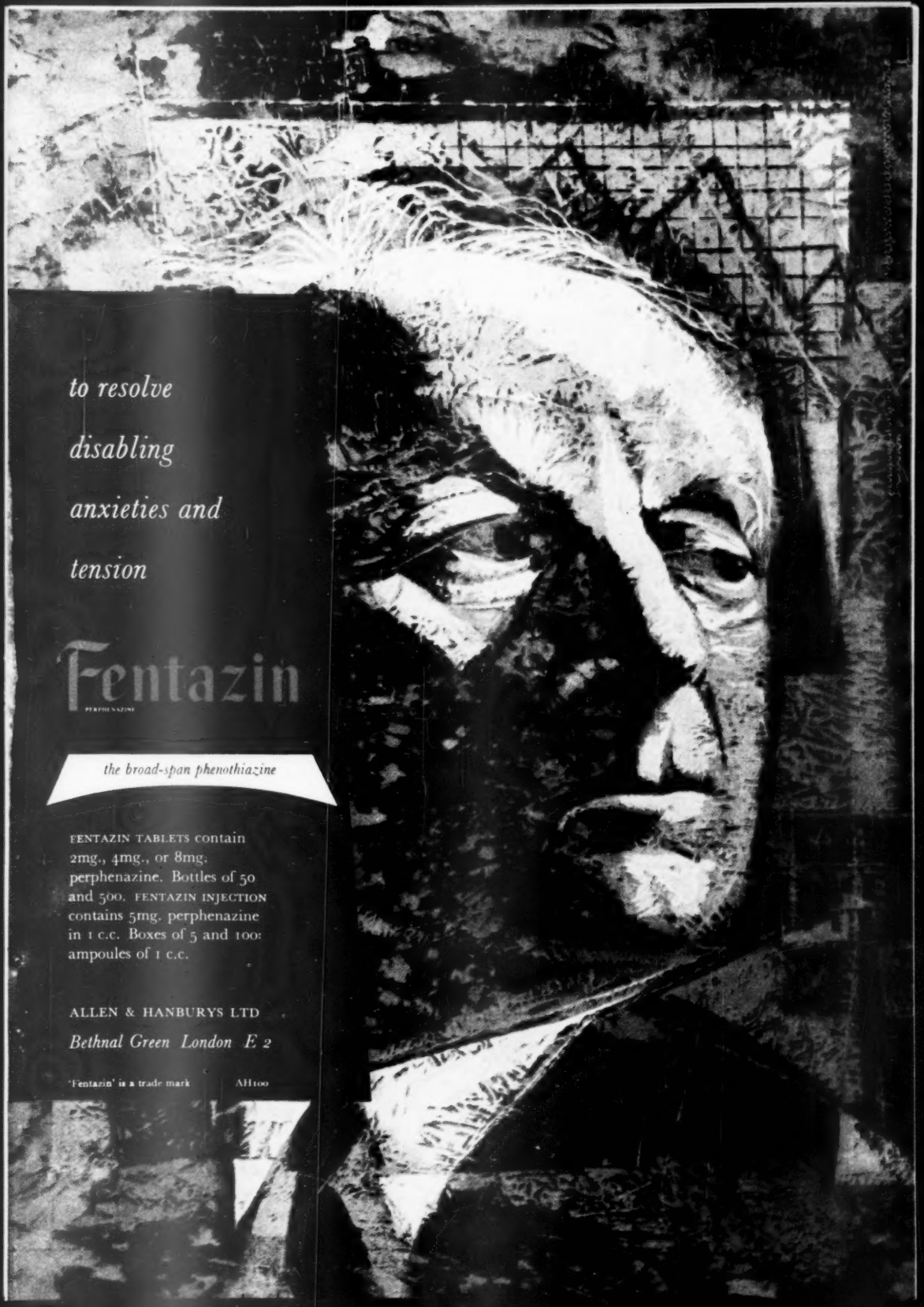
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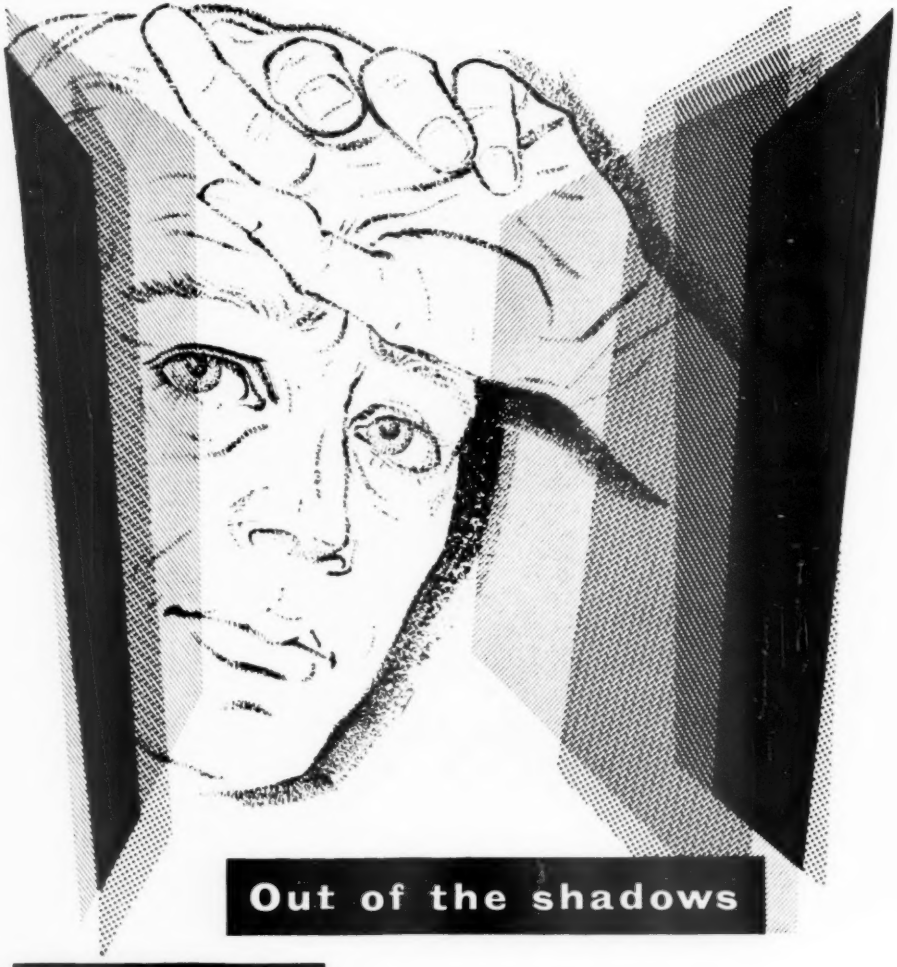

Dartalan

SAFE AND EFFECTIVE IN

PSYCHOSES Particularly Schizophrenia [1 & 2]

NEUROSES Tension states and patients with obsessional traits

GENERAL MEDICINE Agitated states in the elderly [3]

1. Am.J.Psychiat. 1958, **114,** 1034.
2. A.M.A. Arch. Neurol.Psych. 1958, **80,** 481.
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SEARLE HIGH WYCOMBE, BUCKS.

DA : P39

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Section of Endocrinology

President—Professor F. T. G. Prunty, M.D., F.R.C.P.

Meeting
April 24–25, 1959

Joint Meeting with the Society for Endocrinology, the Society for the Study of Fertility, the Medical Section of the British Diabetic Association, the London Thyroid Club, and the Endocrine Club, Glasgow

Direct Measurement of the Effect of Insulin on the Uptake of Glucose by Peripheral Muscles in Normal Subjects, Diabetics and Acromegalics

By Christopher Hardwick, M.D., F.R.C.P., W. J. H. Butterfield, M.D., M.R.C.P., I. Kelsey Fry, M.R.C.P., and J. H. Briggs, M.R.C.P.

London

During the last two and a half years we have been developing techniques to investigate peripheral glucose metabolism and we have already reported some of our findings elsewhere (Butterfield *et al.*, 1958; Butterfield and Holling,1959).

When we realized that small doses of insulin injected into the brachial artery were fixed in the forearm tissues, we thought it would be of interest to measure the direct effect of insulin on the local tissue glucose uptake. In this paper we present our findings so far, in a group of control subjects, and in some selected diabetic and acromegalic patients. Our experimental method has been as follows:

After fasting overnight, the patients or control subjects lie comfortably in bed in the ward. Fine polythene catheters are introduced into the brachial artery through a thin-walled needle and also into a vein draining the deep muscular compartment of the forearm. These permit repeated sampling from both sites for indefinite periods.

When sampling, 1 ml. blood is withdrawn from the artery and vein simultaneously at a steady rate over a period of one minute. Weighed aliquots—weighed to prevent bias during analysis—are used for glucose estimations, using the glucose oxidase method of Huggett and Nixon (1957). After four pairs of fasting samples have been withdrawn, a small dose (0·03–0·1 unit) of glucagon-free insulin, in 2 ml. of normal saline, is injected into the brachial artery over a period of two minutes; using these small doses there is no systemic lowering of blood sugar so that the arterial level remains steady. A wrist cuff, at 200 mm.Hg, is applied during the injection to ensure that the insulin reaches the tissue being studied. After the injection of insulin, arterial and venous samples are withdrawn at intervals of 5, 10, 15, 20, 30 and 40 minutes. The wrist cuff is applied for one minute before sampling and during sampling to exclude blood from the hand and so avoid contamination of the venous samples by arterial blood passing through the numerous arteriovenous anastomoses in the fingers. While the samples are being withdrawn a venous occlusion plethysmograph is used to determine forearm blood flow. Grant and Pearson (1937) first pointed out that this may vary from minute to minute and, in our experience, there may be as much as a threefold variation during an experi-

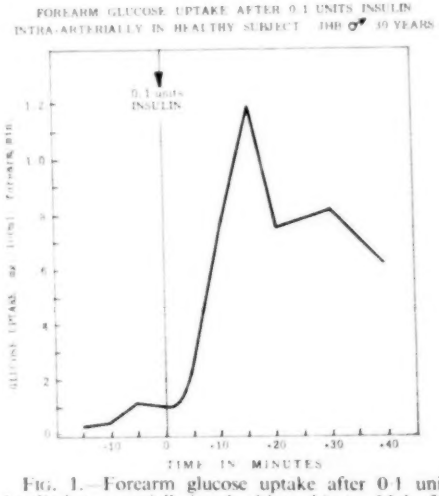

Fig. 1.—Forearm glucose uptake after 0·1 unit insulin intra-arterially in a healthy subject. Male, 30 years.

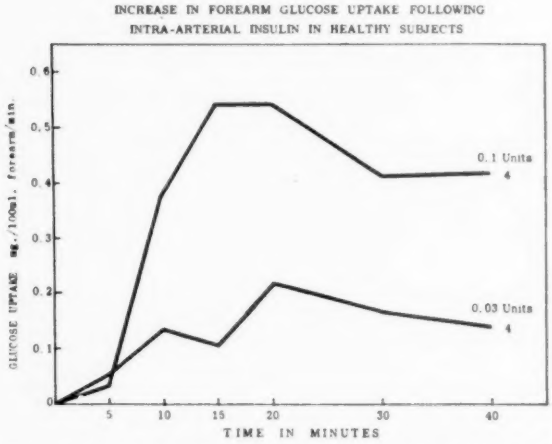

FIG. 2.—Mean increase in forearm glucose uptake above the fasting level following intra-arterial insulin in 4 healthy subjects.

ment. The tissue glucose uptake may be calculated by multiplying the arteriovenous glucose difference by the blood flow and we express it in mg./100 ml. forearm/minute.

The tissue glucose uptake before and after 0·1 unit of insulin in a healthy, 30-year-old male is shown in Fig. 1. It will be seen that the glucose uptake, initially low before the intra-arterial insulin, rose to high levels within 20 minutes of the injection.

Fig. 2 compares the effects of 0·1 and 0·03 unit of insulin injected intra-arterially in control subjects. The two curves represent the mean results from four healthy male subjects. The upper curve refers to the rise in uptake above the fasting level after 0·1 unit of insulin and it will be seen that the mean glucose uptake rose by 0·55 mg./100 ml. forearm/minute. The lower curve refers to the mean result after 0·03 unit; it will be seen there was a prompt but smaller rise.

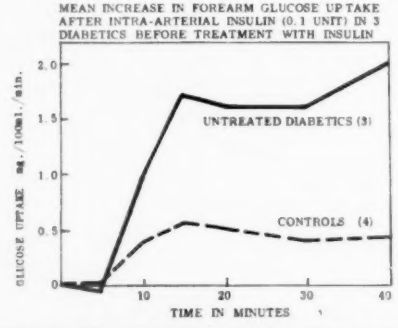

FIG. 3.—Mean increase in forearm glucose uptake after intra-arterial insulin (0·1 unit) in 3 diabetics before treatment with insulin compared with the increase in 4 control subjects. Note change of scale in ordinate.

Findings in selected diabetic patients.—First, recently diagnosed cases who had never received therapeutic injections of insulin: Fig. 3 compares the effects of 0·1 unit of intra-arterial insulin in 3 such cases with the findings in the 4 healthy control subjects. It will be seen that in these diabetics the intra-arterial insulin had a greater effect than in the controls. We attribute this to their high fasting blood sugar, the mean for the diabetics being 170 mg./100 ml. compared with the normals' 86 mg./100 ml.

In marked contrast we have found, so far, diminished responses, despite the high blood sugars, in patients who have been treated for several years with insulin injections. In two insulin-dependent diabetics who had been treated with insulin for twelve and fifteen years respectively, and both of whom were sensitive to insulin clinically, we found no significant response to 0·1 unit insulin intra-arterially. The tests were carried out sixteen hours after the last injection of soluble insulin.

We now turn to a patient with very marked insulin resistance, demonstrated earlier this year to the Pathology Section of this Society on November 18, 1958. The patient was a 60-year-old female who was admitted to East Surrey Hospital in diabetic coma. Diabetes had been diagnosed three years before but the patient soon gave up her insulin injections because of urticaria. In hospital on this

occasion her diabetes and acetonuria were uncontrolled despite very large doses of insulin, ranging up to 2,000 units per day, which again were followed by a rash. When it was suspected that insulin antibodies might be causing the insulin resistance, the patient was treated with prednisolone and some measure of control was achieved.

We had the opportunity to test this patient's peripheral insulin sensitivity shortly afterwards, at a time when her glycosuria was unaffected by 300 units of insulin a day, although her acetonuria had disappeared. 0·1 unit of intra-arterial insulin was without effect on forearm glucose uptake. Our findings are in line with Dr. P. H. Wright's studies of this patient's plasma; using the rat diaphragm technique he found a powerful insulin antagonist. Likewise Dr. A. Cunliffe, of King's College Hospital, using his guinea-pig preparation, found antibodies in this case.

Acromegaly.—It is salutary to remember that prior to 1921 diabetic coma was a common terminal event in acromegaly. Recent experimental studies by Randle and Young (1956) and Wright (1957) have indicated that acromegalic patients may have an insulin antagonist in their plasma. It therefore seemed relevant to determine whether such insulin antagonism would prevent the action of insulin in the periphery. We have investigated this in 8 acromegalics aged 25 to 57 years. A diagnosis of acromegaly was made on clinical and radiological evidence and was always obvious. None of the cases had an associated diabetes; fasting blood sugars were all less than 100 mg./100 ml. From Fig. 4 it can be seen that as a group the acromegalics were insensitive to intra-arterial insulin. Of the 8

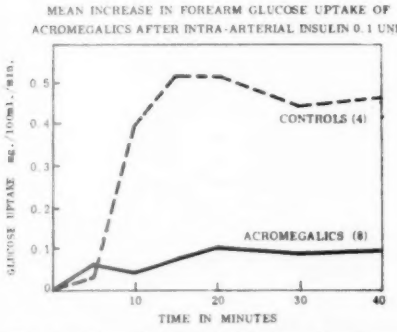

FIG. 4.—Mean increase in forearm glucose uptake after intra-arterial insulin (0·1 unit) in 8 acromegalics compared with the increase in 4 control subjects.

patients, only 1, a 52-year-old female, showed as much response to 0·1 unit insulin as the control subjects. All the others showed some resistance; 2 patients, both males, were completely resistant to as much as 1·0 unit.

We have also had the opportunity to study 3 acromegalics before and after radiotherapy directed at their pituitary glands. All 3 patients showed increased sensitivity to insulin following the treatment.

What is the mechanism of the insulin resistance in acromegalics? The first question we wish to answer is: Does the insulin we inject into the brachial artery escape from the circulation in the way which must occur in the control subjects? We have therefore injected insulin, freshly labelled with iodine 131 into the brachial artery. By following the forearm blood flow during and after the injection and by sampling the effluent vein for radioactivity as well as glucose, we can examine the correlation between insulin fixation and insulin action. These investigations are somewhat complex but we have so far managed to perform six tests in control subjects and acromegalics. Although any opinions expressed in these final remarks must be very tentative, the results do seem of sufficient interest to mention. Control insulin-sensitive subjects trap 60–70% of the radioactivity in the forearm tissues, whereas insulin-resistant acromegalic subjects trap much less, 20–40%. But even in these latter cases it would seem that the injected insulin passes from the circulation into the extracellular space, for some can be detected in the forearm afterwards. By comparison with the normal, it would seem that the fixation of the insulin molecules from the extracellular fluid is impeded.

If we allow that the 20–40% which is retained by the resistant acromegalics represents the amount which passes into the extracellular space in all cases, then there is a rough correlation in the normals between the proportion of insulin trapped and the effect it produces. It would therefore appear that *one* explanation of the insulin resistance of acromegaly is a failure of the cells to accept insulin from the extracellular space. Future work will be directed to testing this hypothesis.

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Toxic Goitre and Abnormal Cardiac Rhythm

By Rupert Vaughan Hudson, F.R.C.S.

London

In 1930 at the request of my colleague, Dr. Evan Bedford, certain euthyroid patients suffering from irremediable cardiovascular lesions and gross cardiac failure were submitted to total thyroidectomy, in the hope that the induced myxœdema would prolong life. The relatively easy operation was eventually performed, under local anæsthesia, upon 24 patients without morbidity or mortality. The diffuse soft small thyroid gland was histologically normal but above the average normal weight. Total thyroidectomy is a misnomer but para-total thyroidectomy expresses the fact that fragments of thyroid tissue are left behind in the neighbourhood of the recurrent laryngeal nerve and the parathyroid glands.

Myxœdema was induced in all, the profundity and clinical characteristics differing from individual to individual. Youth resented myxœdema; the relatives of the elderly resented myxœdema more than the patient. Thyroid extract therefore had to be employed to render the patient para-euthyroid for social and economic reasons. The dose of thyroid necessary varied from individual to individual, and over-dosage rapidly caused return of previous symptoms. Broadly the results were most effective in the reduction of gross œdema. In angina of effort the attacks were diminished in intensity and frequency or abolished. Those with hypertension gave the worst results.

At the same time we were studying the methods to be used in the problem of toxic goitre and cardiac arrhythmia. We had already established that the thyroid crisis could be eliminated by the correct dose of pre-operative iodine. It was therefore decided (1) to perform a radical subtotal or para-total thyroidectomy; (2) to employ sufficient thyroid extract to render the patient para-euthyroid post-operatively; and (3) that the patients, however ill, must be afforded the benefit of surgery.

The pioneer work of Dunhill in 1909, and his publication in 1930 of 100 cases of cardiac arrhythmia, made it evident that the patient suffering from toxic goitre and arrhythmia, however ill, could be assisted by thyroidectomy. From 1930, and before Dunhill's paper was published, and up to 1958, 254 cases of toxic goitre and arrhythmia have been submitted to surgery by our method. Certain observations arise.

Diffuse goitre and nodular goitre.—The complication of arrhythmia is common to toxic diffuse goitre and nodular toxic goitre. In diffuse goitre 144 patients, and in nodular goitre 110 patients, a ratio of 56·7% to 43·3%, suffered from arrhythmia. The average age of the whole group was 51·4 years (in diffuse goitre 48·7 and in nodular goitre 55·0 years).

When we scrutinize 947 cases of diffuse toxic goitre and nodular toxic goitre in normal rhythm, it is found that the average age at which those with severe thyrotoxicosis were operated upon was 38·6 years and 47·9 years respectively.

It would appear that in severe diffuse toxic goitre arrhythmia can follow about ten years after this age, and about eight years in severe toxic nodular goitre. This suggests a period of at least ten to twelve years from the onset of the disease and a severe persistent thyrotoxicosis leading eventually to abnormal rhythm.

As a consequence of the physiological para-total ablation of the thyroid gland, the spontaneous return to normal rhythm was taken as the criterion to measure the surgical result. In the majority this occurred from three to ten days post-operatively coincident with the ablation of the thyrotoxic element, but was delayed occasionally as long as three months. Quinidine was never employed.

Two observations also were made. First, in severe thyrotoxicosis with the onset of paroxysmal auricular fibrillation, the obvious signs of thyrotoxicosis including the eye signs diminished but recurred if normal rhythm spontaneously or temporarily returned with medical treatment. This was most noticeable in moderate and mild thyrotoxicosis and made it difficult to establish clinical evidence of thyrotoxicosis. These features account for the term "masked" hyperthyroidism.

In regard to investigation available at that time the basal metabolic rate was found to be of little practical value in assisting diagnosis in thyrotoxicosis and cardiac arrhythmia. The patients

bedridden and near death might be incapable of performing the test or, if they did so, of giving a normal or nearly normal reading.

Second, in the nodular goitre with very low-grade thyrotoxicosis the removal of a really large goitre, or one causing tracheal narrowing, produced a benefit to the patient out of proportion to the clinical signs of thyrotoxicosis.

In Table I is given the average age and the

TABLE I.—THYROIDECTOMY: THE AVERAGE AGE OF THE PATIENT, AND THE AVERAGE WEIGHT OF GLANDS REMOVED 1930–1958
1,595 CASES

		AGE IN YEARS					
		Diffuse			Nodular		
Type	Total cases	Young-est	Eld-est	Aver-age	Aver-age	Young-est	Eld-est
Cardiac arrhythmias	254	26	71	48·7	55·0	23	81
Severe	710	8	71	38·6	47·9	18	73
Moderate	133	19	63	38·9	43·4	25	68
Mild	104	31	51	43·3	41·4	17	70
Non-toxic	394	26	65	41·0	46·5	17	78

		WEIGHT IN GRAMS					
Type	Total cases	Mini-mum	Maxi-mum	Aver-age	Aver-age	Mini-mum	Maxi-mum
Cardiac arrhythmias	254	20·00	178·00	59·70	130·22	27·00	560·22
Severe	710	16·00	628·00	62·63	102·37	17·00	450·00
Moderate	133	10·00	266·00	44·88	84·80	12·00	434·00
Mild	104	32·00	147·00	89·50	101·69	19·00	342·00
Non-toxic	394	45·00	454·00	131·00	155·43	38·00	769·00

average weight of gland tissue removed in those patients who were operated upon for abnormal rhythm, and compared with the ages and weights of patients in normal rhythm.

In Table II the patients are subdivided into

TABLE II.—ARRHYTHMIA AND THYROTOXICOSIS 1930–1958
Total = 254 cases (21·1% of all cases of thyrotoxicosis)
Males = 27·6% (thyrotoxicosis + normal rhythm = 15·0%)

	Diffuse Average age = 48·7			Nodular Average age = 55·0		
Type	No. of cases	No. with normal rhythm	% normal rhythm	% normal rhythm	No. with normal rhythm	No. of cases
All	144	107	74·3	74·5	82	110
Paroxysmal auricular fibrillation or flutter ..	27	27	100	97·1	34	35
Established auricular fibrillation No failure	61	44	72·1	68·6	24	35
Established auricular fibrillation + Failure	48	29	60·4	64·7	22	34
Established auricular fibrillation + Gross failure ..	8	7	87·5	33·3	2	6
Mortality ..	3	=	2·1%	2·7%	=	3

groups according to whether they suffered from paroxysmal fibrillation or established auricular fibrillation together with a degree of cardiac failure. It can be seen that spontaneous return to normal rhythm is 100% in paroxysmal auricular fibrillation and steadily declines according to the degree of cardiac failure.

In the main, paroxysmal auricular fibrillation denotes impending permanent arrhythmia, whereas cardiac failure denotes the duration of established auricular fibrillation. It was found that established auricular fibrillation, of over one year's duration, whether accompanied by failure or not, rarely returned spontaneously to normal rhythm after thyroidectomy.

An attempt was made to estimate whether the prognosis was influenced by (*a*) the severity of the exophthalmos in diffuse goitre, or (*b*) in nodular goitre in particular by the size of the goitre and its position. No correlation could be found, nor was there any evidence that the severity of the thyrotoxicosis necessarily influenced the onset of abnormal rhythm or the prognosis after thyroidectomy.

Moreover, it appeared that the agent causing thyrotoxicosis, whether affecting a diffuse or nodular goitre, was of the same nature, the end-results were the same, and there was relatively little difference in prognosis. The results varied according to whether the patient had paroxysmal auricular fibrillation, established auricular fibrillation without failure, or established auricular fibrillation with moderate or gross failure. Cardiac failure was eliminated in 100%, likewise paroxysmal auricular fibrillation.

In established auricular fibrillation without failure 72·1% of diffuse goitre returned to normal rhythm, and in nodular goitre 68·6%.

In established auricular fibrillation with moderate or gross failure spontaneous normal rhythm occurred in diffuse goitre 64·3% and in nodular goitre 60%. Those who did not return to spontaneous normal rhythm could be maintained on a small dose of digitalis.

The recurrence rate.—Sentimentality—rare in a surgeon—or extreme technical difficulty at times leads one to perform a sub-total thyroidectomy in young patients. In spite of the paucity of tissue left behind, there have been four recurrences in diffuse goitre fifteen years post-operatively.

The feature of these recurrences was the return of abnormal rhythm with very low-grade thyrotoxicosis, and in one patient two impalpable remnants giving a high radioactive iodine uptake.

One must conclude that in those patients with abnormal rhythm these recurrences emphasize the necessity for a para-total ablation of the thyroid gland. If the surgeon considers in diffuse goitre that the small size of the gland, or the recurrent remnants, is such that ablation cannot be achieved without morbidity, then medical ablation by radioactive iodine is the correct treatment. If this ablation is not achieved by the radiotherapist, then his recurrence rate will be much higher than that of the surgeon.

Spontaneous normal rhythm.—It must be emphasized that the earliest indication of thyrotoxic arrhythmia is paroxysmal auricular fibrillation which is curable in 100% by thyroidectomy. The longer the established arrhythmia is permitted to persist, the less likely is the return of spontaneous normal rhythm following thyroidectomy. One must conclude therefore that the onset of arrhythmia is an urgent indication for para-total ablation of the thyroid gland by surgery, or, in suitable cases, radioactive iodine therapy.

The second conclusion is: has the toxic goitre and abnormal rhythm been superadded to a pathological cardiovascular system such as hypertension, coronary disease, and valvular disease of the heart?

This occurred in 25% of my 254 cases, and only 33% of these patients spontaneously returned to normal rhythm, but they were all rendered free of cardiac failure, and maintained on a small dose of digitalis.

In 75% of patients no abnormality or change could be found in the cardiovascular system pre- or post-operatively. These patients suffered thyrogenic arrhythmia. In them the spontaneous return to normal rhythm was over 80%.

Toxic goitre patients with established hypertension and cardiac arrhythmia did not live as long as the remaining patients, life being terminated by a hypertensive catastrophe, in the majority a cerebral catastrophe. This is true of toxic goitre and normal rhythm; some patients appeared prone to develop insidiously hypertension post-operatively. Now with the assistance of hypotensive drugs the prognosis should be better.

Antithyroid drugs have little place in the treatment of toxic goitre with cardiac arrhythmia; the condition is far too urgent. They definitely play no part in the pre-operative preparation of such patients.

The maximum tolerance dose of digitalis having been established, the patient was rendered as "dry" as possible by the use of diuretics, and not until then was commenced the relatively rapid and safe pre-operative preparation with 60 mg. haustus iodi[1] three times a day, continued on the average for a fortnight, and in some as long as three weeks. During this time the dose of digitalis in the majority was reduced.

In my series there were 6 deaths (2·4%), this mortality is greatly in excess of that of severe thyrotoxicosis and normal rhythm (0·2%). In 4 cases (66·6%) the cause of mortality was due to a fatal embolus or cerebral catastrophe coincident with the establishment of spontaneous normal rhythm.

This work was initiated and made possible by the active co-operation of my colleague, Dr. Evan Bedford, to whom I am deeply indebted.

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[1]Haustus iodi, Middlesex Hospital Pharmacopœia.

Abnormal Iodoproteinæmia in a Child Bearing a Congenital Goitre

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THE present report concerns a 6-year-old patient with a large congenital goitre, in whom radioiodine investigations have revealed the presence in the serum of an abnormal iodoprotein migrating with the albumins.

The parents of the boy are first cousins. A first child, stillborn, had a large goitre. The patient, born six years later, also had a much enlarged thyroid. Three other children were normal. A sixth child was born in August 1959; he has a large goitre.

The somatic and bone development of the patient was normal. There was no myxœdema, but a profound lack of intellectual development. The large nodular goitre was responsible for a tracheal compression with dyspnœa.

Basal metabolism ±0%. Protein-bound iodine 3 μg.%.

Thyroid auto-antibodies negative (Dr. D. Doniach).

Needle biopsy.—Adenoma with well-differentiated cells, but without any colloid secretion. The vesicles are irregular and separated by a pronounced fibrous stroma. There were no lymphocytes. The possibility of a malignant tumour cannot be excluded (Professor P. Dustin).

Investigations with radioiodine.—Thyroid uptake: two hours 65%, six hours 62·1%, twenty-four hours 76·8%. Thiocyanate administration

(800 mg.) was not followed by a discharge of radioactivity from the thyroid gland.

In the plasma, the conversion ratio at the twenty-fourth hour attained 61·5%:

$$\frac{\text{P.B.}^{131}\text{I}}{^{131}\text{I}} \times 100 = \frac{0{\cdot}252\%}{0{\cdot}410\%} \times 100 = 61{\cdot}5\%$$

The chromatography of the plasma butanolic extracts (seven hours, twenty-four hours, forty-eight hours) in a butanol-dioxane-ammonia solvent system showed only the presence of thyroxine. There was no evidence of mono-, di-iodotyrosine or tri-iodothyronine. No qualitative abnormality of the butanol-soluble iodine fraction could be detected.

The serum proteins were precipitated by the Somogyi technique, washed and reassayed for ^{131}I. The protein precipitate was then treated with hydrochloric acid and extracted with n-butanol, following the method of Owen and McConahey (1956). The extracted precipitate was assayed for ^{131}I.

Butanol extractable iodine[1]: In our patient, only 23% of the P.B.^{131}I was extracted by n-butanol. This result seemed to reveal the presence in the serum of an abnormal iodoprotein, not soluble in n-butanol.

Electrophoresis of samples of the serum, obtained six hours, twenty-four hours, and forty-eight hours after ^{131}I was given, was carried out at pH 8·6. The dried strips, cut into segments, were counted in a well counter. The alpha-globulin and inter-alpha-globulin activity did not exceed the background. The forty-eight-hour serum showed an activity exclusively limited to the albumin. This evidence pointed either to the presence of an abnormal iodoprotein migrating with the albumin, or to a lack of the thyroxine-binding protein migrating in the inter-alpha zone. New investigations were planned to decide between these two possibilities.

Study of serum fixation of radiothyroxine in vitro *and* in vivo.—Two months after the preceding investigations, radiothyroxine was added *in vitro* to serum samples up to the concentrations of 0·12; 0·60; 1·2; 2·4 and 4·8 μg./ml. After two hours' and forty-four hours' incubation, the sera were submitted to paper electrophoresis. The cut strips were counted. In all cases, the radioactivity was divided between the inter-alpha zone and the albumin.

Finally, 65 μg. of labelled thyroxine (500 μc) was injected intravenously. Blood was taken after five and twenty-four hours. Serum electrophoresis again showed a distribution of the radioactivity between inter-alpha-globulin and albumin.

The boy was treated by l-tri-iodothyronine and thyroid extract. The goitre volume was reduced; the compression trouble disappeared. Progress at school seemed to improve.

The hypothesis can be made that a congenital enzymatic defect is responsible for the release into the serum of an abnormal inactive iodoprotein migrating with the albumin. This type of congenital abnormality has been described by DiGeorge and Paschkis (1957) and by De Groot *et al.* (1958).

In our case, however, the presence of the iodine in the albumin could also be interpreted as the result of a low capacity of the thyroxine-binding protein. This concept does not explain the development of the goitre.

We are therefore led to consider a dual abnormality. A thyroid defect would be responsible for the presence of an abnormal thyroprotein in the blood and for a low thyroxine level. The low thyroxine-binding protein value would be considered as the result of a compensation mechanism tending to increase the free thyroxine level. It is indeed remarkable that our patient did not show the typical clinical picture of hypothyroidism in spite of the low protein-bound iodine (P.B.^{127}I : 3 μg.).

[1]B.E. ^{131}I = P.B. ^{131}I (Somogyi) − ^{131}I (extracted precipitate).

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Endocrine Disturbances of Pregnancy and Fœtal Pathology

By J. P. Hoet, J. J. Hoet and A. Gommers

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From clinical facts (Hoet, 1954, 1956; Sindram, 1955; Jackson and Woolf, 1957; Carrington *et al.*, 1957; Hagbard, 1958; Joslin *et al.*, 1959) and experimental investigations (Hultquist, 1948; Bartelheimer and Kloos, 1952; Giroud, 1955; Van Faassen, 1957) it became evident that profound metabolic disturbances of the mother during pregnancy are associated with fœtal pathology. The repetition of hormonal disturbances during pregnancy in the same woman and repeated

pregnancy wastage suggest causal relationship (Murphy, 1947; Lilienfeld, 1953; Warkany, 1957). As a rule, major evidence of endocrine disease will, however, be lacking as gross pathology will not allow pregnancy. On the other hand, the past history of an elderly diabetic woman will show perinatal wastage twenty years before manifest diabetes. It is therefore important to look for concealed disturbed carbohydrate metabolism during pregnancy, in any woman with fœtal pathology.

Our study brings a practical answer to the problem stated by Davis and Potter (1957): "It is not uncommon to find individuals who have no living children, or perhaps one child following a number of unsuccessful pregnancies. Women bearing a malformed child often have such histories. Thus, infertility, abortion, stillbirth, neonatal deaths and malformations may be interrelated. The woman with an unsatisfactory reproductive history is likely to be still trying to obtain a child as she approaches those critical years at the end of her reproductive life-time when the incidence of abnormal babies is unusually high. Whether the malformed baby is the result of environmental factors, abnormal hormonal support, nutritional inadequacies, systemic disease or poor genes, or whether all of these factors play interrelated roles, is a question that can rarely be answered in an individual case."

About 1,000 patients came under our care mostly during pregnancy or during their puerperium because of a continuous fœtal wastage. The clinical recognition of metabolic disturbances revealed two insufficient regulatory mechanisms: a prediabetic period during pregnancy and a hypothyroid pattern. This confirmed that there is a close association between these two common hormonal insufficiencies and the fœtal wastage. After the clinical recognition of a metabolic disturbance, cases have been selected for follow-up study during substitution therapy. This study evaluates chiefly the rescue of the fœtus from the fatal consequences of the mother's metabolic disease.

We report chiefly on the results of the glucose tolerance test (G.T.T.), B.M.R. and the examination for night vision during pregnancy or the puerperium of 930 cases with continuous fœtal wastage.

The glucose tolerance test was performed with 100 g. glucose. Capillary blood was taken at three-quarters, one and a half, two and a quarter, and three hours and the blood sugar was determined with the Hagedorn-Jensen method. The presence of true glucose in the urine was looked for with the glucose-oxidase paper method.

The glucose tolerance test was taken as normal if the blood glucose at 0 hours was 1·00 g.; at ¾ hour 1·80 g.; 1½ hours 1·30 g.; 2¼ hours 1·20 g.; 3 hours 1·00 g.%.

The glucose tolerance test results may be grouped in three categories: flat, delayed and prediabetic.

The basal metabolic rate is determined by the standard procedure (Sanborn apparatus). The blood is analysed for liver function tests, cholesterol, P.B.I., blood group and Kahn test. The night vision is tested by a Goldman-Weekers adaptometer.

Table I lists the chief symptoms for which the patients were investigated.

TABLE I.—PERINATAL PATHOLOGY OF 675 PATIENTS EXAMINED FOR CONCEALED ENDOCRINE DISTURBANCES

During gestation—	%
With glycosuria { primipara / multipara }	29
Miscarriage { single / repeated }	22
With macrosomia fœtalis	19·2
With children with congenital malformations	7·8
Neonatal mortality	16
Diabetic heredity only	1·7
Gestation pathology	3·5

As an example of the laboratory findings, the results of G.T.T. during the post-partum period of 29 women who had had a child with congenital malformation gave 8 normal, 4 flat, 11 delayed and 6 prediabetic curves. This indicates that the birth of a malformed child may be associated with a disturbed glucose tolerance test *post partum*. The normal test does not preclude an abnormal carbohydrate metabolism during pregnancy. Therefore the glucose tolerance test in mothers of malformed children was analysed during a subsequent pregnancy.

In 100 women who had previously had a malformed child, other pathological obstetrical histories were often found. 26 of the 100 women had had only 1 malformed child whereas 74 had had associated continuous wastage as well (Table II). This shows that pregnancy wastage may take different aspects. There is in the history of the patients a continuum of obstetrical events. This covers a variety of pathological features: miscarriages, macrosomia, stillbirths and malformed infants.

TABLE II.—THE OBSTETRICAL PAST HISTORY OF 100 WOMEN HAVING MALFORMED CHILDREN

26 Women with one Malformed Child only.	
74 Women with Associated Obstetrical Pathology.	
(*a*) Several malformed children	50%
(*b*) Miscarriage	30%
(*c*) Stillborn	30%
(*d*) Prematurity	32%
(*e*) Heavy child	44%

Of these 100 women, each with a malformed child, 58 became pregnant again and they were

TABLE III.—RESULTS OF GLUCOSE TOLERANCE TEST DURING PREGNANCY OF 58 WOMEN HAVING DELIVERED A CHILD WITH A CONGENITAL MALFORMATION PRIOR TO TREATMENT

G.T.T. curves	No. of pregnant women	Previous pregnancies				
		Polycystic kidneys	Cardiac malformations	C.N.S. abnormal	Other malformations	Total No. of pregnancies with malformations
Normal ..	7	1	2	3	1	7
Flat	18	4	3	8	9	24
Delayed ..	19	—	2	11	8	21
Prediabetic ..	14	—	3	10	4	17

TABLE IV.—GLUCOSE TOLERANCE TEST IN 85 WOMEN WITH A HISTORY OF STILLBIRTH

	Total	Normal	Flat	Delayed	Prediabetic
During new pregnancy					
A. Preceding pregnancy ended in stillbirth	27	9 (33%)	8 (30%)	8 (30%)	2 (7%)
B. One of the previous pregnancies ended in stillbirth ..	26	10 (37%)	2 (8%)	11 (44%)	3 (11%)
During post-partum period	32	5 (16%)	9 (28%)	9 (28%)	9 (28%)

followed carefully during pregnancy. 7 had a normal, 18 a flat, 19 a delayed and 14 a prediabetic G.T.T. Their previous pregnancies are summarized in Table III.

About 50% of these women show a delayed or prediabetic curve at one time during their pregnancy. It has to be stressed that the delayed and prediabetic curves have been found in patients who later became overt diabetics (Conn, 1958).

In Table IV the results of the glucose tolerance test in 85 patients, each with a history of stillbirths are reported. Here again a high percentage (50%) of features of abnormal carbohydrate metabolism can be found as expressed by a delayed or prediabetic G.T.T. As a result of this clinical observation, we took the opportunity to study the influence of the ætiological treatment on the outcome of pregnancies in women with continuous perinatal wastage.

The selection for substitution therapy was made on the basis of abnormal G.T.T., concealed hypothyroidism and personal or familial anamnesis. Although some individual cases are very striking and were reported previously (Hoet *et al.*, 1956; Hoet *et al.*, 1958) as typical effects of insulin treatment during pregnancy on the fœtal development in a concealed prediabetic environment, a group study is reported here.

Of the 58 pregnant women, the outcome of the pregnancy of 30 women is known so far. The outcome of 87 previous pregnancies in these 30 women was as follows: 29 ended with normal living children, while 58 pregnancies ended with fœtal pathology (stillbirths, miscarriage or malformed child).

After treatment with insulin, in some cases in association with thyroid extract, these 30 women had 36 deliveries of which 33 were normal infants while 3 babies only were lost.

In another group of 25 women reporting because of stillbirth, 60 of the 79 pregnancies terminated with the death of the fœtus prior to the ætiological treatment. 19 pregnancies only ended with a normal baby. 26 subsequent pregnancies of these 25 women were treated and 24 normal living infants were born. 2 were lost; both cases suffered from Rhesus incompatibility which was associated with an endocrine disturbance in the mother.

DISCUSSION

From this data covering the past history, the clinical examination of the patients, the investigation of their carbohydrate and thyroid metabolism and the result of a substitution therapy, concealed endocrinopathies are found to be associated with the existence of a "continuum of reproductive wastage".

The G.T.T. has been a tool to discover the metabolic disturbance in the mother. The substitution therapy, correcting some of the metabolic errors, has brought about an alleviation of the biochemical lesions in the receptor organs like the reproductive system and the fœtus.

From the reported data on the outcome of pregnancy, when under substitution therapy, one may postulate that this therapy is chiefly ætiological. It is not stated, however, which metabolic pathway is primarily affected and how the treatment corrects it. Neither is it possible to state at present if there is a parallel between the severity of the metabolic disturbance, evidenced by the G.T.T. and the damage incurred at the level of the target organs. There seems to be a definite, complex relationship between the carbohydrate metabolism of the mother and the histological and biochemical aspects of the endometrium and the placenta. This aspect of the problem has been submitted to experimental investigation (Ricci, 1958*a* and *b;* Ricci *et al.*, 1958; Vaes, 1958; Vaes and De Meyer, 1957; Brasseur *et al.*, 1958; De Meyer, 1954; Hoet, 1953; Hoet *et al.*, 1957).

In this report, we make no comment on minor symptoms which respond to the treatment: often subjective and objective symptoms disappear when insulin or thyroid extract is administered, for instance nausea, morning vomiting, fatigue and pruritus vulvæ.

During this study, we have noticed and put on record in both endocrine conditions, prediabetes and hypothyroidism, an important symptom: carotenodermia, accompanied with hyperkeratosis. It is easily seen on the soles of the feet, the palms of the hands or the nasolabial folds. The hormonal control of the metabolic production of vitamin A from the available carotene has been investigated in many endocrinopathies, in particular in diabetes and hypothyroidism (Moore, 1957). Based on the hypothesis that the carotenodermia is due to metabolic disturbances in the genesis of active vitamin A, we investigated the nyctalopia in the patients with a pattern of reproductive wastage, with the apparatus of Goldman-Weekers. Many patients had a clear-cut pathological night blindness. This is used as a means to show that vitamin-A insufficiency at the level of the effector organs may exist on another basis than the nutritional intake of a vitamin.

Recently, we have reported the results of the correction of night blindness in endocrine syndromes. In selected cases of prediabetes or myxœdema, insulin or thyroid medication brings the night blindness back to normal limits within the first two to five days of treatment (Hoet *et al.*, 1958).

The metabolic relationship between the endocrinopathies and active vitamin-A metabolism may be relevant at the level of the placenta or of the fœtus.

Experimental embryologists have produced fœtal wastage and congenital malformation in the rat and the pig by nutritional deficiency of vitamin A (Giroud, 1955). The conditioning of the vitamin-A metabolism in the human being by hormonal influences may be the causal relationship between the prediabetic or concealed hypothyroid state and the continuous reproductive wastage.

Other examples of fœtal abnormalities due to endocrine conditions in relation to vitamin-A metabolism are investigated by Millen and Woollam (1958).

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Genetic Factors in Intersexes

By JOHN S. S. STEWART, M.B.

Glasgow

THE usual diagnostic criteria of sex include inspection of external genitalia, exploration of internal genitalia by laparotomy and histological examination of the gonads. Secondary sex characters are of lesser importance in sex diagnosis since it is psychologically essential that a decision be reached long before puberty. Nuclear sexing can provide presumptive evidence about the number of X chromosomes present and a study of sex-linked recessive characters, such as colour blindness, can provide genetic evidence about the number and origin of X chromosomes. The distribution of the different types of colour blindness both in the intersexes and in their families is important. Anomaloscope testing can determine the type of colour blindness and its regularity or otherwise. The chromosomal sex can be determined by examination of germ cells in meiosis or of somatic cells in mitosis. For the latter bone-marrow, skin or other tissues may be used.

Recent advances have clarified our understanding of human intersexes and a more rational clinical classification is now possible. It now seems that in man there are three main types of intersexes: (1) true hermaphrodites; (2) chromosomal intersexes; and (3) pseudohermaphrodites. True hermaphrodites have ovarian and testicular tissue. Nuclear sex may be chromatin positive or negative and genitalia, both internal and external, are usually ambiguous. Their status is uncertain but they may be mosaics. The chromosomal intersexes include examples of chromatin-negative Turner's syndrome and of chromatin-positive Klinefelter's syndrome. The former have only 45 chromosomes and an XO sex chromosomal constitution. The gonad is rudimentary or absent and the phenotype female. The latter have 47 chromosomes and an XXY constitution. The gonad is an abnormal testis and the phenotype is male. In these conditions the term "sex reversal" is inappropriate. The pseudohermaphrodites have nuclear sex and internal genitalia corresponding to the gonad present but external genitalia may be ambiguous or those of the opposite sex. They include genetically determined and environmentally induced conditions. Congenital adrenal hyperplasia (female pseudohermaphroditism) is apparently due to an autosomal recessive factor. Other types of female pseudohermaphroditism are due to virilizing factors during pregnancy. Testicular feminization (hereditary male pseudohermaphroditism) could be due to a sex-linked recessive or sex-controlled autosomal dominant factor. Colour blindness studies may distinguish between these possibilities. Congenital adrenal insufficiency is a type of male pseudohermaphroditism of unknown but possible genetic ætiology.

Several families are at present being studied and will be reported in detail later but preliminary investigations are of interest. A chromatin-negative case of gonadal dysgenesis is colour blind (extreme deuteranomaly). Her brother and maternal cousin are also colour blind and both parents are colour normal. A bone marrow specimen was examined by Miss P. A. Jacobs. The patient has a heteroploid bone marrow with only 45 chromosomes. This suggests that the defect is one of spermatogenesis and that the patient has inherited no sex chromosome from her father. Another colour-blind chromatin-negative patient with gonadal dysgenesis has colour-normal parents and there is a history of colour blindness in a maternal uncle. A third colour-blind patient with gonadal dysgenesis is chromatin-positive and has a colour-blind father. This patient may be a mosaic.

A patient with the clinical features of chromatin-positive Klinefelter's syndrome attended a male infertility clinic. The diagnosis was confirmed by nuclear sexing and testicular biopsy. Fibroblasts from tissue culture were examined by Dr. D. G. Harnden and Dr. C. E. Ford and found to have 47 chromosomes. In Glasgow 52 chromatin-positive patients with Klinefelter's syndrome have had their colour vision tested. All were colour normal.

The chromosomal intersexes have an abnormal sex chromosomal constitution and colour blindness studies must therefore be interpreted with caution. Cases of chromatin-positive Turner's syndrome may be mosaics in whom colour blindness would probably be more common than in females but less common than in males. Mosaicism might lead to the production of irregular colour blindness and offers an explanation, among others, of unilateral colour blindness and of heterozygous manifestations in females. Chromatin-positive Klinefelter's syndrome is apparently caused by non-disjunction, an abnormality of meiosis which produces gametes with two sex chromosomes instead of one. The incidence of colour blindness in the syndrome is apparently greater than that in normal females but less than in normal males. The report of colour-blind cases with colour-normal parents suggests that the X chromosomes of XX gametes may sometimes be derived from the same X chromosome. Some types of inversion could be both the cause of non-disjunction and also the mechanism of securing such a gamete with X chromosomes homozygous for colour blindness. An abnormality of the second meiotic division of oogenesis (Fig. 1) appears simpler and could give

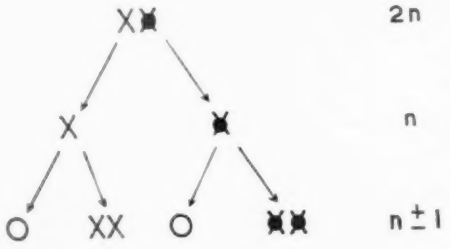


FIG. 1.—Diagrammatic representation of the X chromosomes during oogenesis showing how an abnormality of the second meiotic division may result in a gamete with two X chromosomes homozygous for a sex-linked recessive defect.

the same result and a similar abnormality of spermatogenesis could be the basis for an XYY complex. This might explain data which suggest the possibility of familial transmission of the syndrome. Several mechanisms, which cannot be discussed in detail, are possible and more than one may operate. The most likely alternative cause of colour blindness is recessive homozygosis due to crossing over prior to non-disjunction at the first meiotic division of oogenesis.

A patient with testicular feminization is colour normal. She has a sister who is chromatin negative, colour blind and apparently a case of testicular feminization. Their mother is colour normal and a brother is reputed to be colour blind. This suggests that the condition is due to an autosomal sex-controlled character but it could be sex linked if crossing over has occurred.

A brother and sister with congenital adrenal hyperplasia have been studied. In a sibship of 2 males and 3 females all but 1 male were apparently affected. The affected male, untreated at the age of 36, is apparently fertile since he has a son and this is supported by the patient's seminal specimen. The count of 15 million sperms per millilitre is rather low but quite consistent with fertility.

It seems likely that male type external genitalia imply that androgen of endogenous or exogenous origin has been present during and has influenced development. Two X chromosomes may be necessary for the development of ovarian tissue and testicular tissue may need the presence of a Y. Thus true hermaphrodites may be mosaics of XX and XY or XXY gonadal tissue and could be considered as examples of corticomedullary dysgenesis, one of the chromosomal intersexes. They may turn out to be such a variant of gonadal dysgenesis but are probably best considered as a separate entity until their status is clarified. Chromatin-positive Klinefelter, and chromatin-negative Turner cases appear to be types of gonadal dysgenesis. The former have abnormal testes, apparently of gonadal medullary origin and the latter abnormal ovaries of gonadal cortical origin. They might be called medullary dysgenesis and cortical dysgenesis respectively. In this way a comprehensive scheme for clinical classification can be obtained (Table I) and may

TABLE I.—CLASSIFICATION OF HUMAN INTERSEXES*

True hermaphrodites (cortico-medullary dysgenesis)
- (1) Chromatin positive.
- (2) Chromatin negative.

Chromosomal intersexes (gonadal dysgenesis)
- (1) Chromatin-positive Klinefelter's syndrome (medullary dysgenesis)
- (2) Chromatin-negative Turner's syndrome (cortical dysgenesis)

Pseudohermaphrodites
- (1) Male (testicular feminization)
- (2) Female (congenital adrenal hyperplasia)

*Only the principal types of true and pseudohermaphroditism are shown.

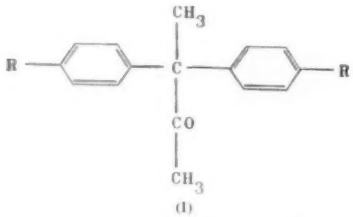
serve as a basis for discussion since revision of nomenclature is required. The status of chromatin-negative Klinefelter cases is still uncertain. They could be caused by involvement of feminizing factors to give an imbalance similar to chromatin-positive cases.

Biological Effects of a Compound Related to Amphenone

By A. C. Brownie, B.Sc., Ph.D., R. B. Hunter, M.B.E., F.R.C.P.Ed., M.R.C.P.Lond., and D. M. Shepherd, B.Sc., Ph.D.

Dundee

Amphenone B, the dihydrochloride of 3 : 3′-bis-(p-aminophenyl)-butan-2-one (I, R = NH_2), suppresses the secretion of adrenal cortical hormones with concurrent adrenal hypertrophy (Hertz *et al.*, 1955).



(I)

It has been used clinically by several workers (Hertz, Pittman and Graff, 1956; Hertz, Renold, Reddy, Pittman, Graff and Thorn, 1956) particularly in cases with adrenal hyperfunction. It is without noticeable effect on the secretion of the normal resting adrenal when given orally. The therapeutic use of amphenone B is limited by its toxicity and by its antithyroid effect.

Chemistry.—We have prepared and studied the closely related compound 3 : 3′-bis-(p-hydroxyphenyl)-butan-2-one (I, R = OH) which, lacking any aromatic amino-groups, would be less likely to produce thyroid enlargement, but might retain the useful properties of amphenone B. This hydroxy compound, hereinafter referred to as HSB I, was prepared by us by treating amphenone B with nitrous acid. On the basis of the original, erroneous formula assigned to amphenone B (Allen and Corwin, 1950; Bencze and Allen, 1957; Korman and Olsen, 1957) we at first regarded HSB I as a new compound, but we subsequently identified it as 3 : 3′-bis-(p-hydroxyphenyl)-butan-2-one which is more readily prepared as described by Adler *et al.* (1944) from p-hydroxyacetophenone pinacol. We have, therefore, obtained further confirmation that the above formula for amphenone B is the correct one.

Animal experiments.—To a group of male rats HSB I (200 mg./kg.) was administered subcutaneously in arachis oil for ten days. Another group received the same dose of amphenone. Table I shows the effect of these compounds on

Table I.—Effect of Amphenone and HSB I on Adrenal and Thyroid Weights of Male Rats

Body wt. at autopsy (g.)	Adrenal wt. (mg.)	Thyroid wt. (mg.)
	Controls	
150	20·5	9·7
167	23·3	10·6
160	17·6	10·0
155	22·2	13·1
	Amphenone	
145	22·3	25·4
150	21·5	36·0
145	24·3	20·2
165	39·6	35·6
	HSB I	
165	27·5	10·4
145	29·6	10·8
160	26·7	12·5
155	33·8	12·2

adrenal and thyroid weights. In agreement with previous workers we found that amphenone administration led to an increase in thyroid and adrenal weights. Adrenal weights of rats given HSB I were significantly increased ($P < 0.02$).

Table II shows the effect of cortisone on

Table II.—Effect of Amphenone and HSB I on Thyroid and Adrenal Weights of Male Rats in the Presence of Cortisone

Treatment	No. of animals	Mean adrenal wt. (mg./kg.)	Mean thyroid wt. (mg./kg.)
Controls	4	87	46
Amphenone	5	117	115
Amphenone + Cortisone	5	89	160
HSB I	5	104	45
HSB I + Cortisone	5	65	53

amphenone- and HSB I-treated male rats. The amphenone and HSB I were given in gum tragacanth suspension by stomach tube in a dose of 200 mg./kg. for ten days. The administration of cortisone acetate (2 mg. daily subcutaneously suspended in 0·2 ml. saline) was started 2 days before amphenone or HSB I. Cortisone suppressed the adrenal enlargement produced by both drugs whereas the thyroid enlargement caused by amphenone was unaffected. Sections of thyroid glands from these groups were stained with hæmatoxylin and eosin. The sections from amphenone-treated rats showed an absence of colloid and the endothelial cell height was increased. The thyroids from HSB I-treated animals gave the normal histological picture of a resting gland with considerable amounts of colloid present, showing no significant difference from the control group.

In acute toxicity studies on HSB I, the oral LD50 for rats was 6·45 g./kg. (limits (P = 0·05) 84–119%), while for mice the intravenous LD50 was 176 mg./kg. (limits (P = 0·05) 86–116%). Death appeared to be due to deep anæsthesia with eventual respiratory failure. Animals frequently remained in deep anæsthesia for twenty-four hours or more before death occurred. In chronic toxicity tests rats which received HSB I (500 mg./kg.) orally each day for eight weeks showed no ill-effects.

Ovariectomized rats were fed HSB I at doses of 0·5 g./kg. and 1 g./kg. for periods up to fourteen days (Table III). The effect on the adrenal

TABLE III.—EFFECT ON HSB I ON OVARIECTOMIZED RATS

No. of animals	Day of treatment	Dose of HSB I (mg./kg./day)	Mean adrenal wt. (mg./kg.)	Mean thymus wt. (g./kg.)	Mean adrenal cholesterol (mg./g.)
4	2	—	102	1·72	40·0
5	5	—	95	1·69	31·3
4	9	—	111	1·57	34·7
4	14	—	85	1·79	24·8
4	2	500	100	1·78	27·3
5	5	500	120	1·74	37·0
6	9	500	109	1·67	40·0
5	14	500	112	1·46	30·8
4	5	1,000	111	2·00	28·7
4	14	1,000	119	1·60	31·9

weight and adrenal cholesterol content was not significant, but when frozen sections of adrenals from these animals were stained for lipid with Sudan III they showed marked lipid accumulation.

Effect of HSB I on urinary steroid excretion by guinea-pigs.—A group of 9 female guinea-pigs, after nine days on a standard diet, had 2% of HSB I incorporated into the diet for ten days. Urine was collected during these periods and also for five days after HSB I administration had been discontinued. The effect of HSB I on 17-ketosteroid (17-KS) and 17-ketogenic steroid (17-KGS) excretion is shown in Table IV. After two days of HSB I treatment the excretion of 17-KGS rose significantly compared with that during the initial control period ($P < 0·05$). When HSB I administration was stopped, the 17-KGS excretion fell sharply. There was no significant change in 17-KS excretion when HSB I was administered, but when HSB I was withdrawn the 17-KS excretion fell ($P < 0·05$). These results

TABLE IV.—EFFECT OF HSB I ON URINARY STEROID SECRETION IN GUINEA-PIGS (GP)

	Mean 17-KS µg./GP/24 hr.	Mean 17-KGS µg./GP/24 hr.
Before HSB I ..	198	146
HSB I	229	207
After HSB I ..	148	130

are similar to the findings of Vogt (1957) who observed increased secretion of corticosterone in amphenone-treated rats.

Clinical trial of HSB I.—HSB I was given orally in doses of 1–8 g./24 hours to patients with breast carcinoma with metastases. These subjects showed normal adrenocortical function as measured by the urinary excretion of 17-KS and 17-KGS. As in the case of amphenone (Hertz, Renold, Reddy, Pittman, Graff and Thorn, 1956), HSB I was found to have no effect on 17-KS or 17-KGS excretion in these subjects.

Effect of HSB I on adrenal response to ACTH.—Figs. 1, 2 and 3 show the effect of HSB I, given orally, on the response of the adrenals to exogenous ACTH in 3 subjects.

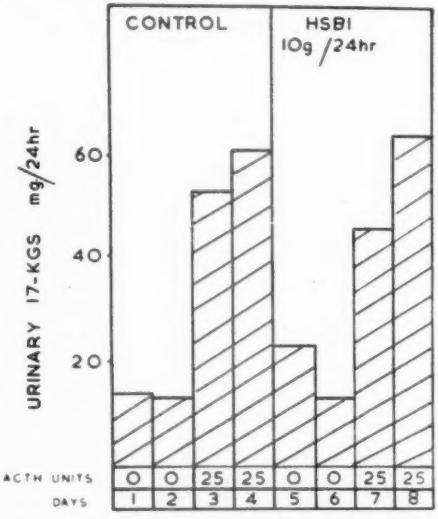


FIG. 1 (*Case I*).—Effect of HSB I on response to ACTH.

Case I.—Woman aged 31 with a history of amenorrhœa. 17-KS and 17-KGS excretion was within normal limits and the response to ACTH was normal. Administration of HSB I, two days before, and during, a second ACTH test produced no apparent effect on the response of urinary 17-KGS excretion to ACTH (Fig. 1).

Case II.—Woman aged 60 with rheumatoid arthritis. The first ACTH test gave a normal response. HSB I given before, and during, the second ACTH test markedly reduced the response to ACTH (Fig. 2).

Case III.—A 44-year-old woman with rheumatoid arthritis. The control levels of 17-KGS were low, but the adrenal responded normally to ACTH. This

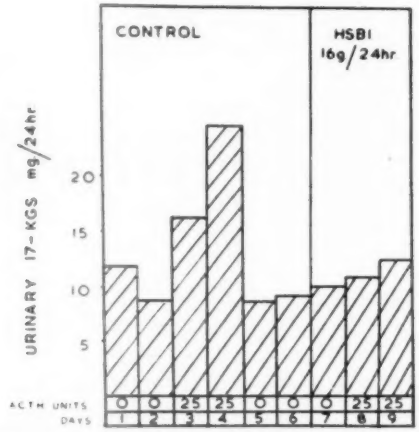


FIG. 2 (*Case II*).—Effect of HSB I on response to ACTH.

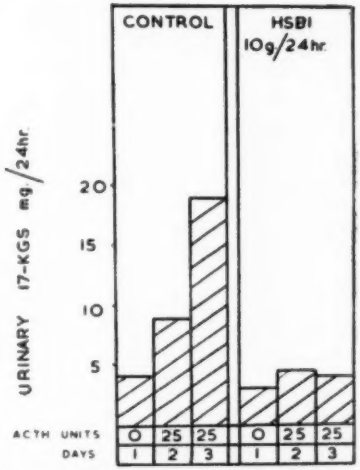


FIG. 3 (*Case III*).—Effect of HSB I on response to ACTH.

response did not occur in the presence of administered HSB I (Fig. 3).

Case IV. A 21-year-old woman with adrenogenital syndrome, in whom control of steroid excretion was achieved with prednisolone, was given HSB I. The drug, administered over a period of four days, significantly decreased the 17-KS excretion, and also affected the difference which existed between the 17-hydroxycorticoid excretion and the 17-KGS. This may indicate an effect on the metabolism of 17-hydroxyprogesterone (Fig. 4).

More recently we have used the compound SU 4885, a specific inhibitor of adrenal 11β-hydroxylase, and studied its effect on adrenal cortical function (Brownie and Hunter, 1959).

Summary and conclusions.—The effect of the compound HSB I on the adrenal has been investigated by animal experiments and clinical trial. Animal studies showed that this compound was much less toxic than amphenone, had no demonstrable effects on the thyroid glands but increased adrenal weight and function to the same extent as amphenone. In normal subjects,

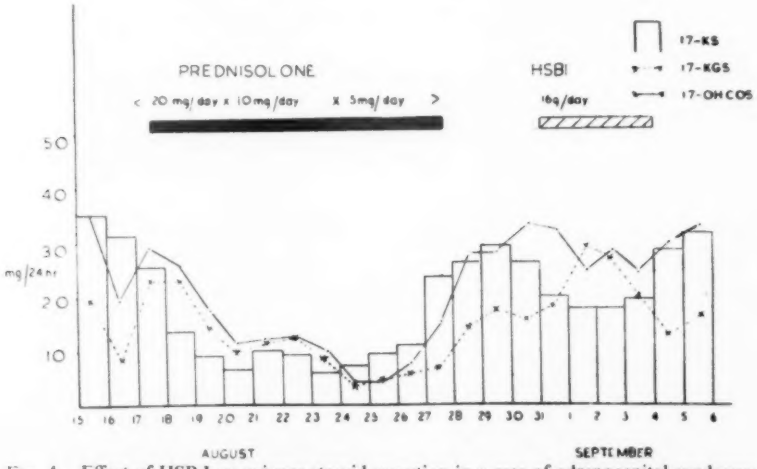


FIG. 4.—Effect of HSB I on urinary steroid excretion in a case of adrenogenital syndrome.

HSB I can reduce the adrenal response to ACTH but this effect is inconsistent. In general HSB I had less activity than amphenone as well as less toxicity.

Acknowledgments.—We are grateful to Organon N.V., Oss, The Netherlands, for the large scale preparation of HSB I, and to Dr. P. B. Marshall who carried out the toxicity tests. We thank Ciba Ltd. for a generous supply of amphenone B.

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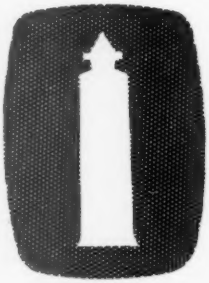

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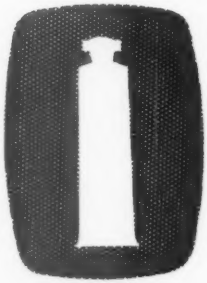

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March 6, 1959

The Evaluation of Premedication in Children

By ANDREW G. DOUGHTY, M.B., F.F.A.R.C.S.
Kingston-on-Thames

THE current trend of preference in the choice of premedication in children appears to be shifting from basal narcosis to pre-operative sedation. This may be due to the growing appreciation of the need to assure rapid recovery from the anæsthetic and to avoid nightmare delirium during the immediate post-operative period (Rees, 1958). The trend is associated with the increasing use of intravenous induction of anæsthesia in preference to inhalational methods even in quite young children. This poses a more complex problem as it implies securing the conscious and willing co-operation of the child.

To achieve this end, all are agreed on the importance of the child's upbringing, the value of a sensible attitude of the parents towards the prospect of his admission to hospital, and the innate tendency on the part of the child himself to co-operate. Also important are a sympathetic attitude on the part of the hospital staff and, in particular, the consideration with which the child is handled by the anæsthetist.

It is in the choice of drugs used to augment the effects of good psychological management that opinions are widely divergent. There are those who maintain that no pre-operative sedative should be necessary (Halstead, 1955), while others report satisfactory results following various combinations of opiates, phenothiazines, euphoriants and tranquillizers, among which may be listed papaveretum-hyoscine (Anderson, 1951; Ballantine and Jackson, 1955), methylpentynol (Rendell, 1954; Gusterson, 1955; Kelsall, 1957), meprobamate (Kern, 1957), pecazine (Green, 1959), and trimeprazine (Cope and Glover, 1959). There is little general agreement as to their relative merits or even as to the optimum doses of each.

The purposes of this communication are: (1) To suggest a means of evaluating methods of pre-operative sedation in children, and (2) To show why reliable observers may come to varying conclusions as to the merits and demerits of any particular method of premedication.

Results are presented of observations on a series of 318 children, most of whom underwent adenotonsillectomy. Their ages ranged from 2 to 12 years, and all were anæsthetized by means of a standard dose of thiopentone 50 mg./stone, and suxamethonium 5 mg./stone. They were intubated and maintained at a light level of anæsthesia with nitrous oxide, oxygen and a trace of halothane, trichloroethylene, or ether.

They were given one of three methods of premedication, designated throughout this paper by capital letters as follows: (1) Atropine Only, (2) Papaveretum-Hyoscine, (3) Methylpentynol-Hyoscine (Table I).

TABLE I.—METHODS OF PREMEDICATION

Drugs	Dosage	Timing	Route	Symbol
Atropine Only	1/100 grain (0·6 mg.) irrespective of weight	30 min. pre-op.	Sub-cutaneous	AO
Papaveretum (Omnopon) and Hyoscine	1/18 grain per stone (0·5 mg./kg.) and 1/900 grain per stone (0·01 mg./kg.)	90 min. pre-op.	Sub-cutaneous	PH
Methylpentynol (Oblivon Elixir) and Hyoscine	1 fl. dram (3·7 ml.) (231 mg.) per stone (36·3 mg./kg.) and 1/300 grain per stone (0·03 mg./kg.)	90 min. pre-op.	Oral	MH

These premedications were selected because their effects are well known, and because of the divergence of opinion as to their efficacy or their safety. Thus one may judge the validity of the method of evaluation by whether or not the known advantages and disadvantages of each premedication are brought to light. The dosages and timing of administration of drugs used in the trial were believed to be effective, but it is not claimed that they were necessarily optimal.

The Atropine Only group was intended to serve as the unsedated "control".

It must be emphasized that the form of premedication must be considered as a whole, not only with reference to the drug given, but to its route of administration, the time that it is given

pre-operatively, and its dosage in relation to body weight. For example, Goulding *et al.* (1957) reported that methylpentynol produced no better results in children undergoing out-patient dental extractions than a similarly coloured placebo. They admitted that the negative results might be attributed to inadequate dosage and incorrect timing, but the over-riding consideration was that the children should recover rapidly from the anæsthetic. Nevertheless, their conclusions have been widely interpreted as meaning that methylpentynol inherently offered no particular advantage as a pre-operative sedative. A more accurate interpretation would be that methylpentynol given in a dose of only 75 mg./stone—the dose then recommended by the manufacturers—only a quarter of an hour before operation, appeared to be of relatively little value. Quite clearly one can only judge the true value of a drug by using it under optimal conditions of dosage and timing.

The dose of methylpentynol given in this series —1 dram (231 mg.)/stone—approximates to that recommended by Kelsall (1957); the addition of hyoscine is recommended by Gusterson (1955), but the dose given here is twice that recommended by him. It should be noted that the dose of hyoscine received orally with the methylpentynol is three times that which would be given subcutaneously to a child of similar weight receiving Papaveretum-Hyoscine. The hyoscine is given primarily for its antisalivary effect, but it may be expected to have euphoriant, anti-emetic and amnesic effects in addition. The dosage of Papaveretum-Hyoscine approximates to that recommended by Anderson for general surgery (1951), and the author has described its use in anæsthesia for adenotonsillectomy (Doughty, 1957).

The children were allotted one of the three methods of premedication at random; all the anæsthetics were given personally and, at the time the observations on the behaviour of the children in the anæsthetic room were made, the observer was unaware of the form of premedication that any particular child had received. The children were seen beforehand, and were told that they would go to sleep after an injection in the back of the hand. A promise to hold the hand quite still during the injection was elicited from each child. The prospect and experience of an injection in the anæsthetic room was used as a legitimate, mildly unpleasant standard stimulus for the purpose of assessing the effect of the premedication.

Three observations were made on each child in the anæsthetic room: (*a*) Demeanour up to the time of the injection, (*b*) Change of facial expression in response to the injection, (*c*) Presence or absence of hand-withdrawal following the injection.

Demeanour in the Anæsthetic Room

Demeanour was recorded in one of six categories: Sleepy, cheerful, serious, apprehensive, tearful and noisy (Table II).

TABLE II.—DEMEANOUR OF CHILDREN IN ANÆSTHETIC ROOM FOLLOWING PREMEDICATION

		Atropine Only	Papaveretum Hyoscine	Methylpentynol-Hyoscine
Satisfactory	Sleepy	0	12	8
	Cheerful	31	24	47
	Serious	38 (69)	39 (75)	37 (92)
Unsatisfactory	Apprehensive	19	28	11
	Tearful	12	1	1
	Noisy	6 (37)	2 (31)	2 (14)
		106	106	106

Statistical observations:

Cheerful/Not cheerful

AO & PH χ^2 = 1·22.	$P < 0{\cdot}30$.	Not significant.
AO & MH χ^2 = 5·20.	$P < 0{\cdot}05$.	Significant.
PH & MH χ^2 = 11·22.	$P < 0{\cdot}001$.	Highly significant.

Satisfactory/Unsatisfactory

AO & PH χ^2 = 0·78.	$P < 0{\cdot}50$.	Not significant.
AO & MH χ^2 = 13·66.	$P < 0{\cdot}001$.	Highly significant.
PH & MH χ^2 = 8·16.	$P < 0{\cdot}01$.	Highly significant.

Those recorded as sleepy were usually rousable but found difficulty in keeping their eyes open. Only one child was not rousable—he had received Methylpentynol-Hyoscine. Some children who had received Atropine Only were asleep on arrival in the anæsthetic room, but on being aroused had no difficulty in keeping their eyes open.

Those recorded as cheerful were those in whom there was no sense of strain whatever, who laughed or smiled readily, were often very talkative, and willing to sing songs or recite nursery rhymes.

The serious category were mixed. They included those who were solemn and not easily amused, or those who may have been apprehensive, but who gave no positive sign of it.

Into the apprehensive group were placed those children who appeared worried; those who looked anxiously around the room; those who seemed anxiously inquisitive about the prospect of their injection, or were disturbed by the appearance of the anæsthetic machine. There were some who volunteered that they were frightened. Others appeared at first to qualify for the cheerful category, but their expression changed to one of dismay when approached with the syringe. Some tried to draw their hand away, but were ultimately persuaded to co-operate.

The tearful children were those who were obviously upset, but were not crying out loud, and in the noisy category were those who were heard before they were seen.

The results of these observations are shown in Table II. It will be noted that despite what might be considered heavy dosage of Papaveretum-Hyoscine and Methylpentynol-

Hyoscine, only 12 and 8 children respectively were classified as sleepy.

It is worth noting the high proportion of those in the Methylpentynol-Hyoscine series whose demeanour was recorded as "cheerful". This contrasts with the correspondingly low figure recorded for Papaveretum-Hyoscine, and is also significantly higher than the figure for Atropine Only. It is difficult to say what contributed to the apparent euphoriant effect of Methylpentynol-Hyoscine. The action of the methylpentynol itself, that of the hyoscine, and the absence of an injection associated with the premedication all have to be considered. Also worth noting is the surprisingly high number of those in the Papaveretum-Hyoscine series noted as "apprehensive", although the number of "tearfuls" and "noisies" are very low—exactly the same as with Methylpentynol-Hyoscine. There is a significantly higher proportion of "tearfuls" and "noisies" in the Atropine Only series.

A dividing line has been arbitrarily drawn in Table II, and those in the sleepy, cheerful and serious groups have been regarded as satisfactory, and those in the apprehensive, tearful and noisy groups as unsatisfactory. This arbitrary line results in children premedicated with Methylpentynol-Hyoscine showing a significant improvement in demeanour over those premedicated with Atropine Only and Papaveretum-Hyoscine. Between Papaveretum-Hyoscine and Atropine Only there is little difference.

It is possible that the less sensitive observer is not prepared to recognize signs of apprehension, and the shedding of tears is necessary to convince him that a child is upset. If this standard were adopted, a very high proportion of the children premedicated with Papaveretum-Hyoscine and with Methylpentynol-Hyoscine would be considered satisfactory, and would show a highly significant improvement over those premedicated with Atropine Only.

It is worth recalling that two years ago, the author made this statement: "Papaveretum-Hyoscine ensures that the child comes to the theatre, not necessarily asleep, but quiet, happy and sufficiently co-operative to allow the anæsthetist to perform venepuncture with ease. . . . At the time of the injection there is seldom any show of fear on the part of the patient" (Doughty, 1957).

An explanation of this inconsistency may be that one's standards become more exacting with the passage of time and that there may be a greater readiness to diagnose apprehension in the children. It is a salutary reminder of the importance of remaining in ignorance of the drug given when making a purely subjective observation and illustrates the necessity of judging different methods of premedication concurrently according to the same criteria.

Response to Venepuncture

Anæsthesia was induced with thiopentone given through a very fine needle, each needle being new or resharpened before use. The response to venepuncture was classified in one of five categories (Table III). Firstly—No response—that

TABLE III.—RESPONSE TO VENEPUNCTURE

		Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Satisfactory	No response ..	52	62	56
	Winced	13	13	24
	Audible response	23 (88)	22 (97)	18 (98)
Unsatisfactory	Started crying ..	16	8	8
	Violent response: Venepuncture abandoned ..	2 (18)	1 (9)	0 (8)
		106	106	106

Statistical observations:
Satisfactory/Unsatisfactory
AO & PH $\chi^2 = 3{\cdot}44$. $P < 0{\cdot}10$. Not significant.
AO & MH $\chi^2 = 4{\cdot}38$. $P < 0{\cdot}05$. Significant.
PH & MH $\chi^2 = 0{\cdot}06$. $P < 0{\cdot}90$. Not significant.

is, no change of expression on the child's face. Secondly—Winced, but no audible response. Thirdly—Audible response—that is, an exclamation or a sharp intake of breath. These can be regarded as satisfactory responses, the criterion being that they are compatible with the normal behaviour of an adult in the same circumstances. In the fourth group are the chil' who started crying following venepuncture, nd of course time was allowed for crying to begin before injecting thiopentone. In the fifth group are the rare cases in whom venepuncture had to be abandoned on account of lack of co-operation.

As might be expected from its analgesic effect, Papaveretum-Hyoscine, as it were, scores the highest for "No response", but it should be noted that Methylpentynol-Hyoscine and Atropine Only show almost as high a proportion—not significantly less than Papaveretum-Hyoscine. Taking the figures for "satisfactory" and "unsatisfactory" in this test, it will be seen that Papaveretum-Hyoscine and Methylpentynol-Hyoscine are almost equal in effect, with the latter just significantly better than Atropine Only. It might be tempting to use this test by itself as a criterion of the success or otherwise of the premedication, yet all but 2 of the 28 classified as "apprehensive" in the anæsthetic room following Papaveretum-Hyoscine were satisfactory by this test. Quite clearly the response to venepuncture can be taken only as part of the evidence on the effect of the premedication.

Hand-withdrawal

As the success of an intravenous induction depends on the patient allowing the anæsthetist to enter a vein with his needle, it is felt that the failure of the child to hold his hand still after being asked to do so should be taken as evidence of unsatisfactory behaviour. Table IV shows the results of observations on the presence or absence of hand-withdrawal following venepuncture. The significant improvement on this test shown by children premedicated with Methylpentynol-Hyoscine will be noted.

TABLE IV.—INCIDENCE OF REFLEX HAND-WITHDRAWAL FOLLOWING VENEPUNCTURE

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Satisfactory: No hand-withdrawal ..	84	93	96
Unsatisfactory: Hand-withdrawal ..	22	13	10
	106	106	106

Statistical observations:
Satisfactory/Unsatisfactory

AO & PH $\chi^2 = 2{\cdot}77$.	$P < 0{\cdot}10$.	Not significant.
AO & MH $\chi^2 = 5{\cdot}58$.	$P < 0{\cdot}02$.	Significant.
PH & MH $\chi^2 = 0{\cdot}44$.	$P < 0{\cdot}70$.	Not significant.

The presence or absence of hand-withdrawal not only tests the ability of the child to co-operate with the anæsthetist, but may also act as a control on the dosage of premedication received. If the child receives a dose of sedative which so clouds his consciousness that the anæsthetist is unable to establish rapport with him in the anæsthetic room, it seems likely that hand-withdrawal will occur following the injection in the back of the hand. Following the report by Galley and Trotter (1958) it seems that children sedated with quite small doses of barbiturate would show a high proportion of failures in this test.

CLASSIFICATION AS SATISFACTORY OR UNSATISFACTORY

It is now possible to classify the patients as "satisfactory" and "unsatisfactory" in the three premedication groups, as shown in Table V. A child who showed unsatisfactory behaviour in any one of the three tests—demeanour in the anæsthetic room, response to venepuncture, or hand-withdrawal—was classified as "unsatisfactory". Those classified as "satisfactory" showed satisfactory behaviour in all three tests.

TABLE V.—CLASSIFICATION OF CHILDREN AS SATISFACTORY OR UNSATISFACTORY BASED ON THE TESTS DETAILED IN TABLES II, III AND IV

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Satisfactory ..	61 (57·5%)	68 (64·1%)	83 (78·4%)
Unsatisfactory ..	45 (42·5%)	38 (35·9%)	23 (21·6%)
	106	106	106

Statistical observations:
Satisfactory/Unsatisfactory

AO & PH $\chi^2 = 0{\cdot}97$.	$P < 0{\cdot}40$.	Not significant.
AO & MH $\chi^2 = 10{\cdot}48$.	$P < 0{\cdot}01$.	Highly significant.
PH & MH $\chi^2 = 5{\cdot}17$.	$P < 0{\cdot}05$.	Significant.

In the first place, one must note the high proportion of children (57·5%) in the Atropine Only group who satisfied these fairly stringent standards of behaviour. Of those premedicated with Papaveretum-Hyoscine, 64·1% were satisfactory. Seen by itself, this figure might appear impressive, but only when considered in relation to the behaviour shown by the children in the Atropine Only group does one realize that credit may be due more to the stoicism of the children than to any special merit of Papaveretum-Hyoscine. The results show clearly the significant superiority of Methylpentynol-Hyoscine over Atropine Only and Papaveretum-Hyoscine. It should be borne in mind that a significant difference between Papaveretum-Hyoscine and Atropine Only might be demonstrated if a greater number of cases were investigated, or if different criteria of behaviour were adopted. Again the method of interpreting the results may not be sufficiently sensitive.

There may be some substance in this criticism in view of the fact that the child who merely exhibits very slight hand-withdrawal would be classed as unsatisfactory equally with a child who exhibited unsatisfactory behaviour in all three tests. A fairer way of estimating the relative value of the three methods of premedication might be to allot each child three points. If a child showed only one unsatisfactory feature, it would score one unsatisfactory point and two satisfactory points, whereas the child who fails all three tests would score three unsatisfactory points.

Table VI shows the points scored for each method of premedication, and it will be seen that the score obtained for Papaveretum-Hyoscine has, as it were, shifted away from Atropine Only towards that obtained for Methylpentynol-Hyoscine. It is not quite certain how these results should be analysed statistically, neither is it felt that the allotment of points would commend itself to the majority of anæsthetists in this country in spite of its popularity elsewhere. Most would say that one is dealing with patients, and either a child is satisfactorily premedicated or it is not. One feels, too, that when judging any method of premedication, its merits should stand

TABLE VI.—EVALUATION OF THE THREE METHODS OF PREMEDICATION ACCORDING TO A POINTS SCORE

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Satisfactory ..	241 (75·8%)	265 (83·3%)	286 (89·9%)
Unsatisfactory ..	77 (24·2%)	53 (16·7%)	32 (10·1%)
	318	318	318

out even though assessed by a relatively insensitive criterion.

It is worth recalling, however, that the main reason why Papaveretum-Hyoscine appears to be less satisfactory than expected, is that a considerable number of children were recorded as showing definite signs of apprehension in the anæsthetic room. If one is not prepared to accept that signs of apprehension are sufficient grounds for "failing" the premedication, then entirely different results will be obtained as shown in Table VII. Here, adopting different criteria, it

TABLE VII.—CLASSIFICATION OF CHILDREN AS SATISFACTORY OR UNSATISFACTORY AS IN TABLE V, BUT ASSUMING THAT "APPREHENSIVES" IN TABLE II ARE NOT CONSIDERED UNSATISFACTORY

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Satisfactory ..	70 (66·0%)	91 (85·8%)	90 (84·9%)
Unsatisfactory ..	36 (34·0%)	15 (14·2%)	16 (15·1%)
	106	106	106

Statistical observations:
Satisfactory/Unsatisfactory

AO & PH χ^2 = 13·66.	$P < 0·001$.	Highly significant.
AO & MH χ^2 = 12·34.	$P < 0·001$.	Highly significant.
PH & MH χ^2 = 0·05.	$P < 0·90$.	Not significant.

can be shown that there is little to choose between Papaveretum-Hyoscine and Methylpentynol-Hyoscine, and both are very significantly better than Atropine Only.

One must, however, reject on principle any attempt to alter retrospectively standards of evaluation decided upon at the beginning of a clinical trial merely because the findings are unexpected or unpalatable. In any case, if a child appears apprehensive in the anæsthetic room, most observers would agree that it is not satisfactorily premedicated.

For the purpose of further discussion, the original evaluation shown in Table V has been adhered to.

AGE IN RELATION TO BEHAVIOUR

It is common belief, confirmed by Goulding *et al.* (1957), and demonstrated statistically by Morton (1957), that young children tend to be less co-operative than older children. It is important, therefore, before drawing firm conclusions from Table V, to ensure that the ages of the children in each premedication group are comparable.

In Table VIII are shown the average ages of

TABLE VIII.—AVERAGE AGES OF CHILDREN IN THE THREE PREMEDICATION GROUPS CLASSIFIED IN TABLE V

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
All cases ..	6·55 SD ±2·34	6·65 SD ±2·34	6·40 SD ±2·1
Satisfactory ..	7·08 SD ±2·50	6·57 SD ±2·22	6·59 SD ±2·04
Unsatisfactory	5·82 SD ±1·93	6·79 SD ±3·92	5·70 SD ±2·22
Difference	1·26 years	0·22 years	0·89 years

Statistical observations:
Mean Ages—Satisfactory/Unsatisfactory

Atropine Only ..	$t = 2·92$.	$P < 0·01$. Highly significant.
Papaveretum-Hyoscine ..	$t = 0·32$.	$P < 0·80$. Not significant.
Methylpentynol-Hyoscine ..	$t = 1·75$.	$P < 0·09$. Not significant.

children in each premedication group. The close similarity of the mean ages and of their standard deviations confirms that the three premedications were allotted to substantially similar age ranges of children.

To test the hypothesis that a child's behaviour improves with advancing years, the mean ages of the satisfactory and the unsatisfactory cases are compared. In the Atropine Only group there is a highly significant difference between the means, but in those children who had received Methylpentynol-Hyoscine, no significant difference is observed. In the Papaveretum-Hyoscine group the mean ages of the satisfactory and unsatisfactory children are almost equal. It is therefore only in the unsedated children that increasing age is associated with a marked improvement in behaviour. As a corollary, one might expect that it should be comparatively easy to achieve a significant improvement in behaviour by sedating the younger children, but a premedication would have to be very impressive in effect significantly to improve the behaviour of older children.

Table IX shows a more detailed analysis of the children according to age and to the premedica-

TABLE IX.—CLASSIFICATION OF CHILDREN IN THE THREE PREMEDICATION GROUPS ACCORDING TO AGE AND BEHAVIOUR

	Atropine Only		Papaveretum-Hyoscine		Methylpentynol-Hyoscine	
	Under 7	Over 7	Under 7	Over 7	Under 7	Over 7
Satisfactory	31 (50%)	30 (68%)	39 (67%)	29 (60%)	42 (72%)	41 (85%)
Unsatisfactory ..	31 (50%)	14 (32%)	19 (33%)	19 (40%)	16 (28%)	7 (15%)
	62	44	58	48	58	48

Statistical observations:			
AO — Under 7/Over 7.	$\chi^2 = 3·49$.	$P < 0·10$.	Not significant.
PH — Under 7/Over 7.	$\chi^2 = 0·53$.	$P < 0·50$.	Not significant.
MH — Under 7/Over 7.	$\chi^2 = 2·61$.	$P < 0·20$.	Not significant.
Under Sevens			
AO & PH	$\chi^2 = 3·66$.	$P < 0·10$.	Not significant.
AO & MH	$\chi^2 = 6·32$.	$P < 0·02$.	Significant.
PH & MH	$\chi^2 = 0·37$.	$P < 0·50$.	Not significant.
Over Sevens			
AO & PH	$\chi^2 = 0·60$.	$P < 0·30$.	Not significant.
AO & MH	$\chi^2 = 3·87$.	$P < 0·05$.	Significant.
PH & MH	$\chi^2 = 7·60$.	$P < 0·01$.	Highly significant.

tion received. Within each premedication group one cannot demonstrate that the children over 7 behaved significantly better than those under 7, but it seems possible that, if more observations were made, such a conclusion might be justified in the Atropine Only group. This contrasts with the highly significant difference in this group between the mean ages of satisfactory and unsatisfactory children (Table VIII). This illustrates the point that a genuine difference may be concealed by the application of an inappropriate statistical test. The error arises from the failure to take into account that increase in years is a gradual process, and that the mere passing of the seventh birthday is unlikely to have a perceptible effect on behaviour.

In the younger children, Methylpentynol-Hyoscine shows a significant improvement over Atropine Only. Between Atropine Only and Papaveretum-Hyoscine the difference falls only fractionally short of the minimum conventional standard of significance. The difference between Papaveretum-Hyoscine and Methylpentynol-Hyoscine in young children is negligible.

In the older children, Methylpentynol-Hyoscine is just significantly better than Atropine Only, but shows a highly significant improvement over Papaveretum-Hyoscine. No evidence can be adduced from these figures to suggest that behaviour in children over 7 after Papaveretum-Hyoscine is significantly different from that after Atropine Only. It is, therefore, doubtful whether Papaveretum-Hyoscine is the most suitable premedication for children in this age group (Cope and Glover, 1959).

Effect of Exposure to Psychic Trauma

In some hospitals, particular care is taken to shield the children awaiting operation from the sight and sound of those returning from the theatre. With the present series, owing to lack of accommodation, it was impossible to take this very humane precaution. Nevertheless, the mingling of the pre- and post-operative children afforded the opportunity of studying the effect on behaviour of this particular form of psychic trauma. It will be understood that the first two children on the list would not be exposed to psychic trauma, while those coming to the theatre later in the list would have heard and seen their predecessors return. During the first half of the series the younger children were brought to the theatre first, while latterly the older children preceded the younger on the list.

Table X is derived from Table IX, but shows the children classified according to age, behaviour, and whether or not exposed to psychic trauma. An inspection of the figures fails to reveal any definite suggestion that exposure to psychic trauma in any way affected the behaviour of the children. This was surprising, as it is certain that a few of the children were, in fact, upset by seeing their comrades return from the theatre. The number of those affected, however, must have been too small to exert any marked effect on the figures. It is worth drawing attention to the highly significant difference between Methylpentynol-Hyoscine and Papaveretum-Hyoscine among the older children exposed to psychic trauma. It is also worth noting the significant difference between the young children after Atropine Only and after Papaveretum-Hyoscine in the "Not exposed" section. This suggests that those who deal mainly with children under 7, and are able to take the precaution of isolating the post-operative patients from those awaiting operation, are justified in having some confidence in Papaveretum-Hyoscine as a premedication.

It may be concluded that oral Methylpentynol-Hyoscine is a reasonably effective premedication. The value of Papaveretum-Hyoscine is that it reduces crying in the anæsthetic room, but it does not mask the less overt signs of apprehension. It cannot be said whether pharmacology accounts for the difference between the two methods, or whether it is simply a matter of the difference in mode of administration.

Criticism of premedication may also be based

Table X.—Classification of Children According to Age, Behaviour, and Exposure to Psychic Trauma

	Atropine Only		Papaveretum-Hyoscine		Methylpentynol-Hyoscine	
Not exposed to psychic trauma	Under 7	Over 7	Under 7	Over 7	Under 7	Over 7
Satisfactory	14 (45%)	12 (67%)	21 (72%)	15 (65%)	23 (68%)	16 (80%)
Unsatisfactory ..	17 (55%)	6 (33%)	8 (28%)	8 (35%)	11 (32%)	4 (20%)
	31	18	29	23	34	20
Exposed to psychic trauma	Under 7	Over 7	Under 7	Over 7	Under 7	Over 7
Satisfactory	17 (55%)	18 (69%)	18 (62%)	14 (56%)	19 (79%)	25 (89%)
Unsatisfactory ..	14 (45%)	8 (31%)	11 (38%)	11 (44%)	5 (21%)	3 (11%)
	31	26	29	25	24	28

Statistical observations:
No significant differences between comparable groups in "EXPOSED" and "NOT EXPOSED" categories.

Note.—PH and MH, Over 7, "EXPOSED", $\chi^2 = 7{\cdot}53$. $P < 0{\cdot}01$. Highly significant.
AO and PH, Under 7, "NOT EXPOSED", $\chi^2 = 4{\cdot}58$. $P < 0{\cdot}05$. Significant.

on unsatisfactory behaviour both during and after the operation. It is therefore necessary to pursue the scrutiny of the three premedications until after the children have recovered from the anæsthetic.

Observations During Operation

During the operation an attempt was made to observe any respiratory depression which might have been due to the premedication. The picture was, of course, complicated by the thiopentone and suxamethonium induction which might have been responsible for a delay in the resumption of normal respiration. However, in the control (Atropine Only) series, only one patient was apnœic at the end of operation. This may have been due in part to over-ventilation, as spontaneous respiration followed the administration of nikethamide and a little carbon dioxide. In the Methylpentynol-Hyoscine series, despite high dosage, only one child was apnœic *until* the end of the operation, when adequate spontaneous respiration started and no further action was necessary. With Papaveretum-Hyoscine, occasional difficulty with respiration was experienced. Nalorphine was given to 6 patients who were apnœic or hypopnœic at the end of operation; normal respiration was restored immediately. A further 4 children were apnœic until the end of operation, when apparently normal respiration returned and no antidote was given. One child who had received Papaveretum-Hyoscine as premedication became extremely restless during recovery in the ward. Nepenthe in the customary dose of 1 minim per year of age was given. Soon after, respiration became alarmingly depressed, but was immediately restored to normal following intravenous nalorphine. This case resulted in the nursing staff becoming somewhat cautious in their dosage of Nepenthe following Papaveretum-Hyoscine, although they adhered to the customary dosage following Atropine Only or Methylpentynol-Hyoscine.

Among the less serious instances of respiratory depression were 7 cases in whom a certain "sensitivity" to halothane was noted. By this is meant that when halothane was being given in small traces with the nitrous oxide and oxygen, spontaneous respiration ceased. It recommenced on turning off the halothane, followed by a few moments of manual compression of the reservoir bag; but when a trace of halothane was reintroduced spontaneous respiration again ceased. It is felt, therefore, that premedication with Papaveretum-Hyoscine may render the management of a patient on nitrous-oxide, oxygen, and a trace of halothane a little more difficult than with other inhalational agents.

The other observation made during the operation was that of the inadequate drying effect of the hyoscine which had been given orally with the methylpentynol. In many of the patients in this group, the surgeon had to use suction to remove a considerable quantity of secretion from the pharynx after inserting the Boyle-Davis gag. This observation suggests that the anæsthetist who wishes to give ether as the main anæsthetic might find himself in some difficulty if he trusted to the anti-secretory effect of this dose of hyoscine given by mouth. It should be remembered that the dose of hyoscine received orally by the children in the Methylpentynol-Hyoscine group was three times that received by a child of the same weight by injection in the Papaveretum-Hyoscine series. In the latter, little trouble with secretions was noted, apart from the occasional slippery mouth. In this connexion, Root (1959) has observed that hyoscine is effective as a salivary drying agent in an intramuscular dose of 0·013 mg./kg., while a dose of 0·055 mg./kg. is necessary to suppress salivary secretion if given orally.

Post-operative Observations

Post-operatively, observations were made by the ward sister on vomiting, restlessness, crying and the need for post-operative sedation. Owing to the varying timing or mode of administration of the three methods of premedication, it was not possible to keep her in ignorance of the drugs which each individual child had received. Observer bias may, however, have been partly eliminated by the deliberate switching of the inhalational agent given with the nitrous oxide and oxygen between halothane, trichloroethylene and ether.

It may be considered unfair to judge the effect of various premedications on the vomiting rate following adenotonsillectomy. It can be held that a child may vomit more on account of swallowed blood rather than any factor connected with the anæsthetic. Again, post-operative pain is probably greater after this operation than after many others so that one might expect an abnormally high incidence of crying and restlessness. Nevertheless, it should be realized that by far the majority of fit children subjected to anæsthesia are for adenotonsillectomy; it seems reasonable, therefore, to judge post-operative behaviour against the background of this operation.

It is with these reservations that the post-operative findings are presented, and their possible implications are discussed in general terms rather than on the results of precise statistical calculations. Excluded from these observations are those of children on whom

TABLE XI.—POST-OPERATIVE VOMITING

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Not vomited	45 (48%)	40 (48%)	51 (56%)
Vomited once	21 (23%)	17 (20%)	15 (16%)
Vomited repeatedly ..	27 (29%)	27 (32%)	25 (27%)
	93	84	91

Vomiting rates in relation to premedication and to inhalational agent given.

	Halothane			Trichloroethylene			Ether		
	AO	PH	MH	AO	PH	MH	AO	PH	MH
Not vomited ..	17 (57%)	21 (64%)	17 (52%)	19 (63%)	9 (39%)	14 (54%)	9 (27%)	10 (36%)	20 (63%)
Vomited ..	13 (43%)	12 (36%)	16 (48%)	11 (37%)	14 (61%)	12 (46%)	24 (73%)	18 (64%)	12 (37%)
	30	33	33	30	23	26	33	28	32

NOTE.—A difference of 25% between comparable observations in samples of about 30 cases may be tentatively regarded as significant at the 5% level.

adenoidectomy or antrum washout only was performed, those who were subsequently returned to the theatre for arrest of reactionary hæmorrhage, and those who had received nalorphine to counter respiratory depression following Papaveretum-Hyoscine.

Post-operative vomiting (*Table XI*).—The patients were originally put into three categories: "Not vomited", "Vomited once", and "Vomited repeatedly". An inspection of the figures reveals no very striking difference between the vomiting rates in the three premedication groups, so for more detailed analysis, the patients have been categorized as simply "Not vomited" and "Vomited".

If the vomiting rates are classified in relation to premedication and to the inhalational agent given, three interesting points emerge: (1) the vomiting rates after halothane are relatively unaffected by the premedication given, (2) the vomiting rates after Methylpentynol-Hyoscine are relatively unaffected by the inhalational agent given, (3) the highest vomiting rate after Atropine Only and Papaveretum-Hyoscine and the lowest vomiting rate after Methylpentynol-Hyoscine are associated with ether anæsthesia. This is particularly interesting as no one has suggested that atropine "makes them sick", although this charge has been levelled against Papaveretum-Hyoscine (Gusterson, 1958). An alternative explanation might be that the ether "makes them sick" and that the large dose of oral hyoscine given with the methylpentynol helps to prevent vomiting. There is good reason to believe that the use of halothane in preference to ether might significantly reduce the incidence of vomiting where oral hyoscine is not given with the premedication.

Restlessness and crying.—Separate observations on restlessness and crying were made, but the overall figures which resulted were similar, except that throughout the three premedication groups "restlessness" was a more frequent observation than "crying" (Tables XII and XIII). As might be expected, the use of Papaveretum-Hyoscine is associated with fewer "restless" and "crying"

TABLE XII.—POST-OPERATIVE RESTLESSNESS

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Not restless	15 (16%)	39 (46%)	17 (19%)
Restless	78 (84%)	45 (54%)	74 (81%)
	93	84	91

Restlessness in relation to premedication and to inhalational agent given

	Halothane			Trichloroethylene			Ether		
	AO	PH	MH	AO	PH	MH	AO	PH	MH
Not restless ..	8 (27%)	18 (55%)	5 (15%)	4 (13%)	12 (52%)	3 (12%)	3 (9%)	9 (32%)	9 (28%)
Restless ..	22 (73%)	15 (45%)	28 (85%)	26 (87%)	11 (48%)	23 (88%)	30 (91%)	19 (68%)	23 (72%)
	30	33	33	30	23	26	33	28	32

NOTE.—A difference of 25% between comparable observations in samples of about 30 cases may be tentatively regarded as significant at the 5% level.

TABLE XIII.—POST-OPERATIVE CRYING

	Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Not crying	30 (32%)	47 (56%)	26 (29%)
Crying	63 (68%)	37 (44%)	65 (71%)
	93	84	91

Crying in relation to premedication and to inhalational agent given

	Halothane			Trichloroethylene			Ether		
	AO	PH	MH	AO	PH	MH	AO	PH	MH
Not crying ..	14 (47%)	23 (70%)	11 (33%)	8 (27%)	13 (57%)	7 (27%)	8 (24%)	11 (39%)	8 (25%)
Crying	16 (53%)	10 (30%)	22 (67%)	22 (73%)	10 (43%)	19 (73%)	25 (76%)	17 (61%)	24 (75%)
	30	33	33	30	23	26	33	28	32

NOTE.—A difference of 25% between comparable observations in samples of about 30 cases may be tentatively regarded as significant at the 5% level.

children than either Atropine Only or Methylpentynol-Hyoscine. In the detailed analysis of the observations on crying and restlessness associated with the inhalational agent, it appears that the sedative effect of Papaveretum-Hyoscine is best seen with halothane and is virtually cancelled out by the use of ether. It appears, therefore, that an observer using ether is likely to come to erroneous conclusions regarding any beneficial effect of premedication on behaviour in the immediate post-operative period. It has been stated (Kenton and Parsons, 1953), that it is desirable to use trichloroethylene during the maintenance of anæsthesia on account of its supposed analgesic effect during recovery. There is no evidence from these figures that such a contention can be sustained.

Post-operative sedation.—Nepenthe was never given prophylactically, the chief indications for its use being crying or restlessness, though it was also given to children who remained peaceful but who complained of pain. Only 5% in the Atropine Only and 10% in the Methylpentynol-Hyoscine groups escaped Nepenthe, whereas 34% of those premedicated with Papaveretum-Hyoscine did not receive it. One must, of course, take into account the cautious attitude of the nursing staff towards giving Nepenthe to children known to have received Papaveretum-Hyoscine as premedication.

Did the Child Mind the Intravenous Injection?

Opinions are still divided as to whether or not an intravenous induction of anæsthesia is to be preferred to an inhalational method. The children in this series were induced intravenously, and the day after operation every child was questioned as follows: (1) "How many pricks did you have?" (2) "Where?" (3) "Did it (or they) hurt?"

The object of this questionnaire was to find out if the child retained any unpleasant memories of the thiopentone injection. The answers are classified in Table XIV.

It will be observed that Papaveretum-Hyoscine appears to be very significantly associated with amnesia for the intravenous injection as compared with Atropine Only, yet 20% of the latter group did not remember the injection. It appears, therefore, that if Atropine Only has no amnesic effect, the whole process of undergoing an anæsthetic must contribute to some extent towards amnesia. It will be noted that with Methylpentynol-Hyoscine the number of cases showing amnesia is neither significantly higher than those in the Atropine Only group, nor significantly lower than those who received Papaveretum-Hyoscine.

Table XIV.—Children's Opinion of Intravenous Induction
Summary of Answers to the Question: "Did the prick in the back of your hand hurt?"

		Atropine Only	Papaveretum-Hyoscine	Methylpentynol-Hyoscine
Satisfactory	Amnesia	21	44	32
	"No"	30 (71)	36 (80)	52 (84)
Unsatisfactory	"A little"	16	10	11
	"Yes"	11	11	8
	Indefinite answer	8 (35)	5 (26)	3 (22)
		106	106	106

Statistical observations:

Amnesia/No amnesia		
AO & PH	$\chi^2 = 11{\cdot}72$.	$P < 0{\cdot}001$. Highly significant.
AO & MH	$\chi^2 = 3{\cdot}04$.	$P < 0{\cdot}10$. Not significant.
PH & MH	$\chi^2 = 2{\cdot}95$.	$P < 0{\cdot}10$. Not significant.
Satisfactory/Unsatisfactory		
AO & PH	$\chi^2 = 1{\cdot}87$.	$P < 0{\cdot}20$. Not significant.
AO & MH	$\chi^2 = 3{\cdot}99$.	$P < 0{\cdot}05$. Significant.
PH & MH	$\chi^2 = 0{\cdot}04$.	$P < 0{\cdot}90$. Not significant.

Nevertheless, it will be seen that a substantial number of children receiving Atropine Only or Methylpentynol-Hyoscine, though remembering the thiopentone injection, denied that it hurt. Although Methylpentynol-Hyoscine is associated with a significantly higher number of satisfactory answers than Atropine Only, the number of satisfactory answers in the latter group is surprising when one considers that the children had the benefit of neither an analgesic nor an amnesic in their premedication.

It may be fair to conclude that those who did not remember the injection, and those who did not mind it, would not object to this method of induction of anæsthesia on a subsequent occasion.

Final Analysis of Results According to Observers of Varying Bias

After reporting the results of observations on children before, during, and after the operation, a fair question to be asked would be "Which of the three methods of premedication is the best?" The only possible reply to this is "It all depends on what is required from the premedication". From the literature, it appears that different observers recommend different methods because they have different criteria of what is acceptable and unacceptable. To illustrate this point, the results of this investigation are analysed in three different ways according to the probable bias of enthusiasts for each of the three methods of premedication.

Those prejudiced in favour of Atropine Only may take this line: "I am satisfied as long as I can get the child to accept an intravenous injection; I do not mind how much he cries or how apprehensive he appears; as long as the intravenous induction is successful, I regard that premedication as a success. I will not tolerate respiratory depression of any degree. I do not mind post-operative restlessness and I welcome crying—it

is good for the children—it expands their lungs, and it shows that it is safe to give them Nepenthe. I do not like them to vomit repeatedly. I am unconcerned with the child's memory of the intravenous injection."

SATISFACTORY—by this criterion:

Atropine Only	66 out of 93 (70·9%)
Papaveretum-Hyoscine.. ..	45 out of 91 (49·5%)
Methylpentynol-Hyoscine ..	65 out of 91 (71·4%)

On this basis, one can make out a good case for Atropine Only being as effective a premedication as Methylpentynol-Hyoscine and with a more satisfactory anti-salivary effect. Both are very significantly better than Papaveretum-Hyoscine.

Those prejudiced in favour of Papaveretum-Hyoscine may argue thus: "I notice that you have failed Papaveretum-Hyoscine because many children gave the appearance of being apprehensive in the anæsthetic room. I cannot accept that one can accurately diagnose apprehension in children under these conditions. Otherwise I agree with your criteria of satisfactory pre-operative behaviour. I am not worried by respiratory depression; one can always respire the patient artificially during the operation and give nalorphine afterwards. Although I do not mind the children vomiting, I do not like post-operative crying and restlessness—it increases the risk of hæmorrhage; nor do I like them to retain an unpleasant memory of the intravenous induction."

SATISFACTORY—by this criterion:

Atropine Only	2 out of 93 (2·2%)
Papaveretum-Hyoscine.. ..	26 out of 91 (28·6%)
Methylpentynol-Hyoscine ..	12 out of 91 (13·2%)

By this rather exacting standard, Papaveretum-Hyoscine shows a significant improvement over Methylpentynol-Hyoscine, while Atropine Only scarcely merits consideration as a premedication.

Those prejudiced in favour of Methylpentynol-Hyoscine may take this view: "I accept your criteria for satisfactory and unsatisfactory behaviour in the anæsthetic room. I will not tolerate respiratory depression. I do not like post-operative vomiting. It is not fair to expect post-operative sedation from the premedication. I can always prevent crying and restlessness by giving Nepenthe at the end of the operation. I do not like the children to retain an unpleasant memory of the thiopentone injection."

SATISFACTORY—by this criterion:

Atropine Only	17 out of 93 (18·3%)
Papaveretum-Hyoscine.. ..	17 out of 91 (18·7%)
Methylpentynol-Hyoscine ..	33 out of 91 (36·3%)

By these standards one can demonstrate Methylpentynol-Hyoscine to be significantly better than Atropine Only and Papaveretum-Hyoscine, and the figures can be interpreted as showing that children premedicated with Papaveretum-Hyoscine are no better off than those premedicated with Atropine Only.

The Ideal Premedication

In attempting to reconcile these three opposing views, one can formulate what may be called "The Ideal Premedication", which, if obtainable, would be acceptable to all.

(1) The child should accept the prospect of venepuncture with equanimity, and should not move or cry at the time of the injection.

(2) The premedication should not be associated with respiratory depression.

(3) The premedication should not be associated with post-operative vomiting, crying or restlessness.

(4) The child should retain no unpleasant memory of the intravenous induction.

If these ideals are applied to the three methods of premedication, it will be found that the following numbers of children behaved satisfactorily before, during and after the operation.

Atropine Only	2 out of 93 (2·2%)
Papaveretum-Hyoscine.. ..	9 out of 91 (9·9%)
Methylpentynol-Hyoscine ..	8 out of 91 (8·8%)

These final figures seem to emphasize that the field is wide open for the introduction of a really satisfactory premedication for children. Meprobamate (Equanil), pecazine (Pacatal), and trimeprazine (Vallergan) are said to be promising. Can they survive with any greater credit the same scrutiny that has been focused on Atropine Only, Papaveretum-Hyoscine and Methylpentynol-Hyoscine?

Summary

Current opinion as to the best form of premedication in children is tending away from basal narcosis towards light sedation. Concurrently, the mode of induction of anæsthesia is tending away from inhalational towards intravenous methods. The requirement is, therefore, a premedication which will enable a child to be sufficiently co-operative and self-controlled readily to accept the prospect and the experience of an intravenous injection.

A method is presented for the evaluation of pre-operative sedation as distinct from basal narcosis. To illustrate the method, observations were made on the behaviour of 318 children before and during venepuncture following one of three different premedications: (*a*) Atropine only—by injection (control group). (*b*) Papaveretum-Hyoscine—by injectiion. (*c*) Methylpentynol-Hyoscine—by mouth.

The results are presented in a form amenable to statistical analysis. According to the criteria defined, Methylpentynol-Hyoscine appears to be a satisfactory premedication whereas Papaveretum-Hyoscine shows little advantage over Atropine Only. Nevertheless that if different criteria were adopted Papaveretum-Hyoscine could also be shown to be highly satisfactory. The effect of age on behaviour is examined, and it is concluded that only in the unsedated children are advancing years associated with a marked improvement in behaviour.

Observations are made on the incidence of respiratory depression associated with Papaveretum–Hyoscine, and figures are presented showing that post-operative restlessness, crying and vomiting are related not only to the premedication received, but to the volatile anæsthetic agent given.

The paper concludes with an analysis of the interpretations which observers of varying bias might place on the figures which have been presented.

Acknowledgments.—My thanks are due to my surgical colleagues Mr. K. G. Rotter and Mr. A. C. Riley for their interest and co-operation; to Sister Bowen, in charge of the Children's Ward at Surbiton Hospital, for observing and recording the post-operative behaviour of the patients; and to Mrs. M. Beckenham, for administrative and secretarial assistance. I am also indebted to Dr. H. J. V. Morton for his interest and advice on the design of the clinical trial and to Dr. J. C. Lees for checking some of the statistical calculations.

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DISCUSSION

Dr. Ronald Green summarized the results of two trials he had conducted comparing the effects of a mixture of the phenothiazine drug—Pacatal (pecazine)—and hyoscine, firstly with Seconal (quinalbarbitone) and atropine in children under 8, and secondly with Omnopon (papaveretum) and scopolamine (hyoscine) in older children in the 8–14 age group. 215 children received Pacatal; 155 received Seconal.

The Pacatal mixture consisted of 1·0 gram of the drug, 0·005 gram of hyoscine and flavouring made up to 100 c.c. and the dose given was 1 c.c. of this mixture per 5 lb. of body weight, equivalent to 2 mg. per lb. (The children given this premedication also received 2 mg. Pacatal per lb. the night before operation.)

The Seconal was given by mouth in capsule form 0·6 grain per stone body weight one hour before operation followed by atropine 1/100 grain half an hour later, by subcutaneous injection.

Omnopon and scopolamine was given by subcutaneous injection one hour before operation in a dose of Omnopon 1/30 grain and scopolamine 1/1000 grain per stone body weight.

As little fuss as possible was made in preparing these children for operation, and those awaiting surgery did not see earlier cases returning from the theatre.

Induction was by thiopentone and halothane for those in the Omnopon and Pacatal groups, while the children who had received Seconal were induced by inhalation with halothane.

All the operations were for tonsillectomy, and anæsthesia was maintained by nitrous oxide, oxygen and ether through a Boyle-Davis gag.

Observations.—(1) In the anæsthetic room: Children asleep or awake but co-operative were recorded as satisfactory; those showing apprehension, or who were noisy or tearful, were classed as unsatisfactory.

(2) During induction of anæsthesia: Children who appeared undisturbed, or who merely winced or whimpered were recorded as satisfactory; those who struggled or cried, or in whom the injection was abandoned were classed as unsatisfactory.

(3) Post-operatively: Patients were recorded as unsatisfactory if they vomited more than once, were sufficiently restless to need physical restraint, were cyanosed or had laryngeal spasm.

Results.—(1) Pacatal and hyoscine compared with Seconal and atropine: Although 60% of the Seconal group were asleep on arriving at the anæsthetic room compared with only 6·5% of those receiving Pacatal, nevertheless about 85% of both groups were recorded as satisfactory in the anæsthetic room. Again there was little difference in their behaviour during induction —over 80% of both groups being satisfactory.

However, the post-operative state was markedly improved in the children who had received Pacatal; only 2½% vomited more than once compared with 15% in the Seconal group, and only 6% were sufficiently restless to require restraint as against 21% in the Seconal group.

The overall results based on the criteria outlined above showed that 75% of the Pacatal series were recorded as satisfactory throughout, compared with 49% of the Seconal series.

(2) Pacatal and hyoscine compared with Omnopon and scopolamine: Over 85% of both groups were recorded as satisfactory in the anæsthetic room and during induction, and over 70% of both groups when the post-operative state was included in the assessment, and there was therefore no significant difference in the two series. However, there was again a noticeable difference in the number of children who vomited more than once post-operatively: 4% in the Pacatal group compared with 17% in those who had received Omnopon and scopolamine.

Dr. W. Donald Munro (Nottingham) suggested that the occurrence of amnesia in a considerable proportion of the series who had had 0·6 mg. Atropine Only might be explained by the similar effect observed in 10-st. adults when given 6 mg. atropine intravenously. He wondered whether the improved results obtained in the Methylpentynol-Hyoscine group might be attributable, chiefly, to the high dosage of hyoscine which was used. He had now been using a considerably increased hyoscine dosage in combination with papaveretum (papaveretum 2·5 mg. and hyoscine 0·1 mg. per stone of body weight) in over 200 children.

There was appreciable improvement on the results obtained with the accepted 50 : 1 ratio of Papaveretum-Hyoscine.

Dr. W. N. Rollason (Hull): In a somewhat similar type of investigation I conducted involving 456 children, whose ages ranged from 1½ to 13½ years, the sexes were fairly evenly distributed, and no relationship between premedication and sex was found.

The premedications in this investigation consisted of:

(i) Syr. chloral 5 grains/stone body weight—119 children.

(ii) Oblivon (methylpentynol carbamate) 100 mg./stone body weight—101 children.

(iii) Phenergan elixir (promethazine) 5 mg./stone body weight—101 children.

(iv) A control series of 135 children who received no premedication at all.

Each premedication was given orally one to one and a half hours before induction of anæsthesia.

All children had a guillotine tonsillectomy and adenoidectomy performed and all received nitrous oxide, oxygen and a trace of trichloroethylene administered by myself.

Each child's behaviour was assessed objectively on presentation of the anæsthetic pre-operatively and again post-operatively on arriving in the ward after leaving the recovery room.

Three categories of behaviour were adopted—calm, disturbed and turbulent. If the child appeared tranquil and unmoved by the proceedings he was classed as calm; if he appeared anxious or cried but responded readily to reassurance he was described as disturbed; if he was completely unco-operative or actively obstructive in spite of attempts at reassurance he was regarded as turbulent.

The children were divided into three age groups: 0–4 years, 5–9 years and 10–14 years.

Pre-operatively, there was no significant difference between those receiving premedication and those receiving no premedication at all in all three age groups.

Post-operatively, comparing those children who received no premedication with those who did, the number showing turbulence was significantly less in those who received no premedication, $\chi^2 = 3{\cdot}84$, $P < 0{\cdot}05$. Comparing the three age groups the number manifesting calm appear to increase with increasing age, $\chi^2 = 5{\cdot}23$, $P < 0{\cdot}10$.

In the dosage range investigated the three premedications showed no improvement on no premedication at all in so far as the objective behaviour of the children was concerned. Indeed the ward staff now prefer the children to have no premedication. Whether or not a current trial with Vallergan (trimeprazine) will cause them to change their view remains to be seen.

Dr. Sheila Anderson: Although Dr. Doughty quoted his dosage of papaveretum and hyoscine as that advocated by me, in fact the dose I use is slightly greater than the one Dr. Doughty was using during this investigation. My own dosage is based on 1 mg. of papaveretum per 3·5 lb. body weight and hyoscine 0·02 mg. per 3·5 lb. body weight. This dosage provides very satisfactory medication for children of 35 lb., that is about 5 and 6 years and upwards.

Premedication by injection should be given by the intramuscular rather than hypodermic route, because an intramuscular injection is less painful, more reliable and takes less time to take effect.

With reference to the induction of anæsthesia, it is unreasonable to submit a small "chubby" child of 2, 3 or 4 years, who has elusive veins, to numerous needlepricks, for the purpose of giving thiopentone, because a very pleasant and peaceful induction of anæsthesia can be produced by using cyclopropane, after which veins become dilated and far more easy to enter.

Dr. F. R. Gusterson: A factor which has not received the emphasis it should is the personality of the anæsthetist and the whole theatre team. When I first took an interest in the premedication of children an E.N.T. surgeon for whom I do not work remarked "I am not so impressed by this new technique as by the fact that an anæsthetist is taking that amount of trouble with children". This remark also applies to Dr. Doughty. Has he allowed for it in his assessment of his methods?

Dr. Doughty (in reply): Dr. Monro's use of a 25 : 1 rather than a 50 : 1 Papaveretum-Hyoscine mixture may well improve the efficacy of the premedication, both as to its euphoriant, anti-emetic, and anti-salivary effect. It is also possible that the respiratory depressant action of papaveretum may be reduced. It would be a valuable contribution if he were to carry out a clinical trial of the two mixtures.

The fact that Dr. Rollason found no difference pre-operatively between chloral, methylpentynol carbamate, promethazine and no premedication at all is open to two interpretations; either the drugs used were inherently ineffective, or the dosage was inadequate.

That Dr. Anderson has recently increased her dosage of Papaveretum-Hyoscine suggests that a trial is long overdue in order to discover the optimum dosage of a potentially valuable combination. I feel that the dose of Papaveretum-Hyoscine which I used (1 mg. papaveretum to 4·2 lb.) was a reasonable maximum considering firstly, the brevity of the operation; secondly, that 11% of the children were somnolent pre-operatively; and thirdly, that some evidence of respiratory depression was observed in no less than 17% of cases. It would be interesting to know if Dr. Anderson would identify her views with those of the hypothetical enthusiast whose opinions are summarized above (page 832).

I do not suggest that an intravenous induction is ideal in all small children; in fact, I agree that attempts to achieve it may be distressing to the patient. In this series an attempt at venepuncture was made in all children simply in order to provide a uniform stimulus against which to test the efficacy of the premedication.

Dr. Gusterson suggests that the personality of those by whom the child is handled may have an effect on behaviour. This may partly explain the variety of opinions of observers using essentially similar dosage of the same drug. It is, therefore, all the more evident that one method of premedication cannot be compared with another unless they are used concurrently by the same observer under the same conditions.

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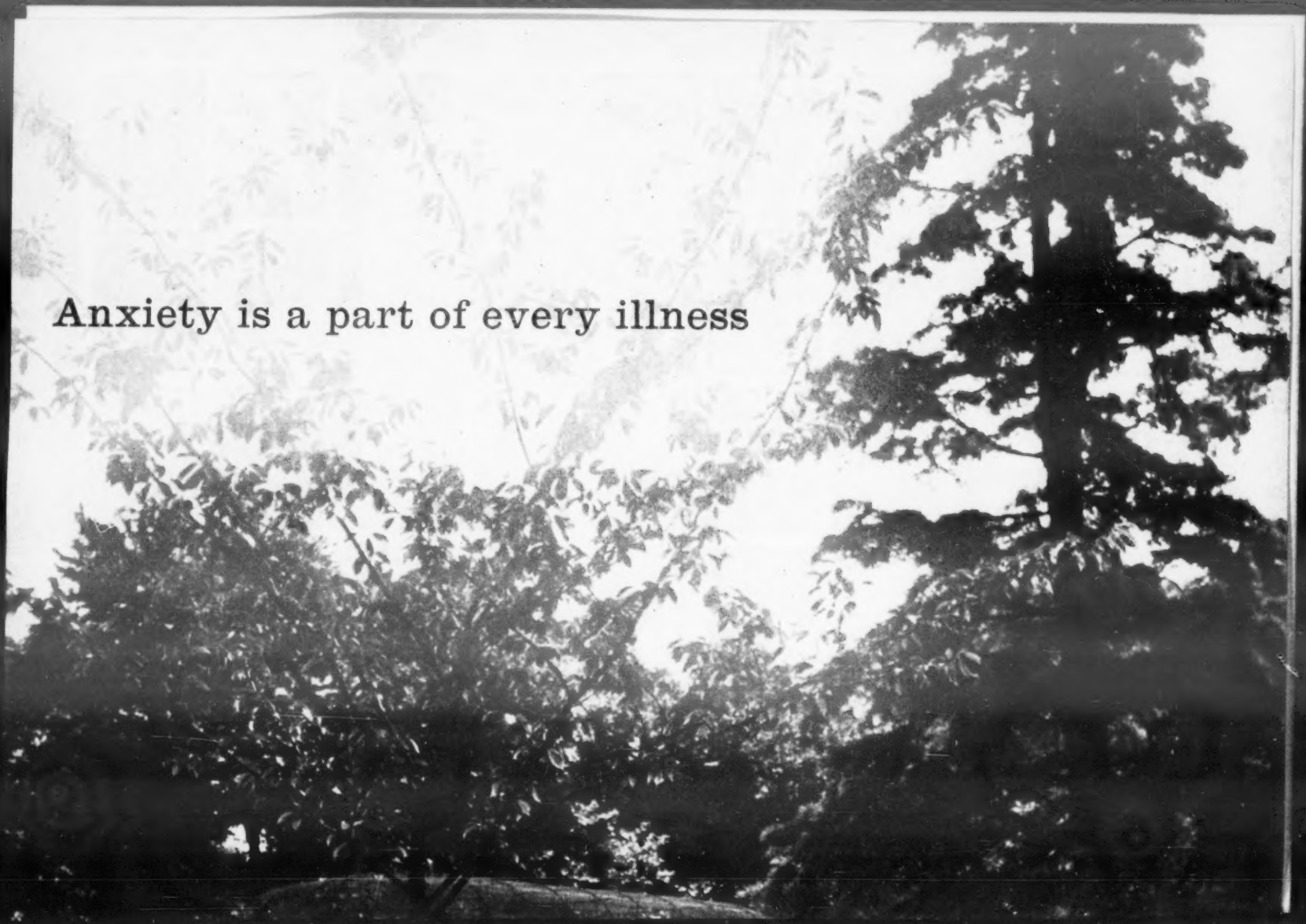
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DISCUSSION ON THE SURGICAL MANAGEMENT OF CHRONIC DUODENAL ULCER

Dr. Lester R. Dragstedt (Chicago):

Gastric Vagotomy for Duodenal Ulcer

The therapeutic value of complete division of the vagus nerves to the stomach in duodenal ulcer depends upon the fact that this operation abolishes the nervous phase of gastric secretion, which markedly reduces the total output of gastric juice by the stomach. It also reduces the tone and motility of the stomach without causing serious complications or side-effects. The first operation was performed in January 1943, and in the intervening years we have operated on 1,400 patients with various types of peptic ulcer in our clinic by this method.

The failure of the gastric and duodenal mucosa to be digested away in normal individuals appears to demand the postulate of a local decrease in resistance, brought about by vascular impairment or other factors, if ulceration is to be accounted for by peptic digestion. The sharply punched-out character of the lesion seemed to support Virchow's suggestion of infarction of the gastric wall. The prompt recurrence of ulceration after local excision, however, casts grave doubt on this view of a decrease in resistance as the causative factor, and careful examination of resected stomachs has also usually failed to reveal evidence of vascular pathology. There is, however, good evidence that the corrosive and digestive properties of the gastric content in ulcer patients are much greater than in normal people. The key to the ulcer problem was probably provided by the demonstration that pure undiluted fundic secretion can digest all living tissues, including the wall of the stomach and duodenum, and produce ulceration exactly like that encountered in patients. When an excessive secretion of gastric juice occurs, the buffering effect of food, saliva, and regurgitated duodenal secretions is overcome and the corrosive properties of the gastric content approach that of pure gastric juice. I should like to present for your consideration the concept that peptic ulcers are usually caused by a hypersecretion of gastric juice: further, that the hypersecretion of gastric juice in duodenal ulcer patients is usually of nervous origin, and that the hypersecretion of gastric juice in gastric ulcer patients is usually of hormonal or humoral origin.

The evidence that duodenal ulcers are usually caused by a hypersecretion of gastric juice of nervous origin may be summarized as follows: (1) Duodenal ulcer patients usually secrete from three to twenty times as much acid in the fasting empty stomach at night as do normal people. (2) If a hypersecretion of acid of this degree is reproduced in experimental animals, typical peptic ulcers regularly appear in the duodenum. (3) Complete division of the vagus nerves to the stomach abolishes this fasting hypersecretion, indicating that it is of nervous origin. It is probable that in some way the tensions and strain of modern life induce a secretory hypertonus in the vagus nerves, and in this way the central nervous system plays a role in the disease. (4) As the fasting hypersecretion in duodenal ulcer patients is abolished by vagotomy, the ulcers usually heal, and if an adequate drainage operation has been added so that stasis of food in the antrum does not occur, they remain healed.

The evidence that gastric ulcers are usually due to a hypersecretion of gastric juice of humoral origin, while not complete, is nevertheless impressive. Experimental data support the validity of Edkin's gastrin hypothesis, namely that the gastric phase of secretion is mediated exclusively by the antrum of the stomach which functions as an endocrine organ, producing and releasing a gastric secretory hormone. Factors causing the release of gastrin from the antrum have been found to be contact of the mucosa with food or the development of tension within the stomach as a result of peristalsis. Excision of the antrum reduces the humoral phase of gastric secretion to a negligible amount, and transplantation of the antrum into the colon as a diverticulum produces a hypersecretion of gastric juice. This hypersecretion is sufficient to cause the development of gastric, duodenal, or gastrojejunal ulcers in the dog, an animal that rarely develops these lesions spontaneously. It is probable that a hypersecretion of gastric juice of humoral origin occurs in man when prolonged stasis of food in contact with the antrum mucosa occurs, as a result either of pyloric stenosis or of deficient gastric peristalsis. Delayed emptying of the stomach has been found in a large proportion of gastric ulcer patients,

and in approximately 20% of these pyloric stenosis from a previous duodenal ulcer has probably caused hypermotility and increased tension within the antrum as well. Experimental data indicate that stasis of food in the stomach due to diminished gastric motility, such as that caused by vagotomy, can produce a hypersecretion of gastric juice of humoral origin sufficient to produce ulceration in the stomach. These concepts are in harmony with surgical experience. Resection of the antrum exerts a curative effect on gastric ulcers, even those left in situ near the œsophagus, and gastrojejunal ulcers rarely develop. On the other hand, antral resection for duodenal ulcer has been followed by a high incidence of gastrojejunal ulceration, and for this reason more extensive resections have been customarily employed. Vagotomy alone has been found ineffective in gastric ulcer patients and when performed for duodenal ulcer has in many cases caused stasis in the stomach with subsequent gastric ulcer formation.

Gastric vagotomy should be performed only in those ulcer patients in whom the nervous phase of gastric secretion is found to be abnormally great as measured by the free hydrochloric acid output in the fasting nocturnal secretion. The fasting secretion is chiefly of nervous origin. The patient is placed on a liquid diet for twenty-four or forty-eight hours to make sure there is no solid food in the stomach. An intragastric nasal tube is introduced at nine o'clock in the evening and continuous gastric aspiration made for twelve hours until nine the next morning. During this time the patient is shielded from the sight, odour, or taste of food and usually sleeps. The volume of the gastric aspirate is then measured and its free acid concentration determined. If the volume is expressed in litres and the free acid concentration in clinical units, the product of the two gives the amount of free hydrochloric acid in terms of milliequivalents. Normal people produce between 15 and 20 mEq. of free hydrochloric acid in the fasting nocturnal secretion in a twelve-hour period. Duodenal ulcer patients may produce from 40 to 350 mEq. If the output is 100 mEq. or greater, the likelihood of medical management proving successful is remote and surgical treatment is probably indicated. Most gastric ulcer patients produce less acid in the fasting nocturnal secretion than normal people, and in these vagotomy should never be performed. There are some, however, who have had a previous duodenal ulcer, in whom the nocturnal acid output is excessive, and in these vagotomy combined with antral resection should be done. The tendency for stasis of food in the antrum to occur after vagotomy demands that antral resection or an adequate drainage procedure be combined with the operation. I have usually recommended a pyloroplasty or posterior gastroenterostomy of small size, with the stoma in the antrum close to the pylorus. Death is the worst thing that can happen to a duodenal ulcer patient, and the mortality of even low gastric resection is four to eight times greater than that of gastroenterostomy. Removal of the antrum is the most certain way to prevent gastric hypersecretion in the vagotomized stomach. I appreciate that gastric resection is being done with an exceedingly low mortality in our leading surgical clinics. However, most of the surgery for ulcer is not performed in these clinics, and this fact must be kept in mind.

Most of the persistent or recurrent duodenal ulcers in our experience have occurred in patients with incomplete vagotomy or with stasis of food in the antrum from an inadequate drainage procedure. Incomplete vagotomy is usually indicated by a twelve-hour nocturnal gastric secretion of more than 20 mEq. of free hydrochloric acid and by a positive secretory response to insulin hypoglycæmia. In a few patients persistent or recurrent ulceration associated with marked hypersecretion of gastric juice has been due to a chemical agent released by a special type of islet cell tumour of the pancreas described by Ellison and Zollinger. A gastrojejunal ulcer may form after complete vagotomy if an entero-enterostomy has been added to the drainage procedure. This diverts the alkaline duodenal secretions away from the gastroenterostomy stoma and produces a situation resembling that which obtains in the Mann-Williamson procedure for the production of experimental ulcers in animals. It is now quite apparent that even a complete vagotomy cannot be relied upon to heal or to prevent this type of ulcer in either man or experimental animals.

The ideas expressed in this brief report are summarized in the proposed classification of peptic ulcers in Table I.

TABLE I.—CLASSIFICATION OF PEPTIC ULCER

A. Hypersecretion ulcers
  (1) Hypersecretion of nervous origin
    (*a*) Duodenal ulcer
    (*b*) Gastrojejunal ulcer
    (*c*) Œsophageal ulcer
  (2) Hypersecretion of humoral origin
    (*a*) Gastric ulcer (excessive liberation of gastrin caused by gastric stasis)
    (*b*) Ellison-Zollinger ulcer (liberation of gastric secretory stimulant from pancreatic tumour)
    (*c*) Ulcer in liver cirrhosis (gastric secretory stimulant from intestine not inactivated by liver (NH_3?)

B. Ulcer without demonstrated hypersecretion (cinchophen, cortisone, and curling ulcer)

Mr. R. L. Holt (Manchester):

Three years ago I took part in a discussion before this Section on the surgical management of uncomplicated duodenal ulcer (Holt, 1956). At that time those of us who supported vagotomy as the most logical treatment accepted the criticism that our results had not been subjected to a sufficiently long test period. This criticism is no longer valid and a steadily mounting volume of evidence has shown that vagotomy is as effective as subtotal gastrectomy in curing duodenal ulcer and in protecting the patient from recurrent ulceration. The problem which confronts the surgeon to-day is not that of curing duodenal ulcer but of making sure that the patient in the process of being cured is restored as nearly as possible to normal, without finding himself troubled with one or more annoying symptoms which are to be found grouped together under the misleading title of the postgastrectomy syndrome. The term is misleading because the symptoms are common to most gastric operations and certainly to any in which the stomach is anastomosed to the jejunum.

At the meeting to which I have referred I reported our results in duodenal ulcer of combined vagotomy and gastrojejunostomy. The high incidence of cure of the original ulcer and the low incidence of recurrent ulceration which were apparent in those results (Table I) have not

TABLE I.—VAGOTOMY AND GASTROJEJUNOSTOMY: TOTAL 358

Operative deaths	2	Subsequent operations	10
Recurrent ulcers	1	Intussusception (1)	
Hæmatemesis	2	Partial gastrectomy (2)	
		Adhesions (1)	
		Pylorectomy (6)	

appreciably altered during the succeeding years. Only one additional case of stomal ulceration has occurred. Stomal ulceration is becoming rare in the Manchester area. In the past eight years only 19 cases of stomal ulceration have been admitted to my unit. Of these, 14 followed a posterior gastrojejunostomy and 5 a Polya type gastrectomy. This is a small number in an area in which duodenal ulcer is very common. Simple vagotomy is an unsatisfactory operation because of the hypotonicity of the stomach and the resultant gastric retention. When combined with gastrojejunostomy, pylorectomy, or pyloric antrectomy, the results of vagotomy in the treatment of duodenal ulcer challenge and in my opinion are superior to those obtained from subtotal gastrectomy.

The important question is: which is the best combination of these procedures? A comparison between the usual type of Polya gastrectomy and a vagotomy combined with a gastrojejunostomy shows that the results of both operations are very good. There is nothing to choose between the two in the cure of the duodenal ulcer and the incidence of stomal ulceration, but there is a slight but definite advantage in favour of vagotomy and gastrojejunostomy when the incidence of post-operative sequelæ is considered. Both operations have in common the complications which follow an anastomosis between the stomach and jejunum. The complications classified under the heading of the postgastrectomy syndrome are: Obstruction at the stoma, diarrhœa, undernutrition, anæmia, postcibal vasomotor disturbance, hyper- and hypoglycæmia, biliary regurgitation. In at least 5 of these 7 complications the main ætiological factor is the rapid emptying of the stomach into the jejunum and the rapid transit through the small intestine of undigested and hypertonic food. X-ray examination shows that a large fraction of a meal may leave the stomach within one minute of being ingested and may reach the ascending colon in twenty minutes.

In 1956 I suggested that to avoid these complications the gastric contents should pass into the duodenum rather than the jejunum, and that vagotomy should be combined with what I called "anterior pylorectomy". There is nothing original about this procedure which is identical with the operation described by Beattie (1950). In Table II are listed the minor sequelæ

TABLE II.—MINOR SEQUELÆ OCCURRING IN 145 PATIENTS FOLLOWING VAGOTOMY AND GASTROJEJUNOSTOMY

	Bilious vomiting	Dumping	Diarrhœa
Severe	3	1	0
Moderate	7	7	3
Slight	12	11	8

TABLE III.—MINOR SEQUELÆ IN 54 MEN AND 11 WOMEN FOLLOWING VAGOTOMY AND ANTERIOR PYLORECTOMY

	Bilious vomiting	Dumping	Diarrhœa
Severe	—	—	—
Moderate	—	—	—
Slight	5 (2 men) (3 women)	3 (1 man) (2 women)	3

following vagotomy and gastrojejunostomy, and in Table III, for comparison, those following the first group of 65 cases of vagotomy and anterior pylorectomy. The results are short-term since none of them is over six years and some only three years. But in my opinion this combination of vagotomy and anterior pylorectomy is much the best treatment for duodenal ulcer. I have done over 150 operations with only one death and that from a pulmonary embolus, so that it is a safe operation. There has been so far no proven case of recurrent ulceration. I have re-operated on 2 patients with an incomplete vagotomy who were complaining of epigastric pain and they are now restored to normal health. I have had to re-operate on 2 patients who subsequently developed a pyloric stenosis due to a technical fault in the early cases and these too

are now completely cured. There has not been, apart from the 4 cases already mentioned, any case in which there have been any serious complications. Equally encouraging is the very low incidence of minor sequelæ. Bilious vomiting, which was our most troublesome complication after vagotomy and gastrojejunostomy, has almost disappeared. The cases of diarrhœa reported amount to no more than an occasional looseness of the stools.

The results in our previous series of vagotomy and gastrojejunostomy were very good. Those of vagotomy and anterior pylorectomy are better. Even in our women patients they are good, for four of the complications occurred in 2 women whose symptoms were probably menopausal. If these results are as good in another five years as they are now we need not worry much more about the treatment of duodenal ulcer. The most convincing evidence of the value of this operation is how well the well patients are. There is no reserve about occasional digestive disturbances; they are restored to normal health. They are eating what they choose, as much as they want, smoking and drinking and working at their old jobs with no loss of time. I have never seen a more satisfied group of patients after a gastric operation. What I am certain of is that vagotomy is at least equal to subtotal gastrectomy in curing duodenal ulcer and preventing subsequent ulceration and that combined with an anterior pylorectomy it provides a very low incidence of subsequent symptoms.

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Mr. George Y. Feggetter (Newcastle upon Tyne): *Treatment of Chronic Duodenal Ulcer by Vagotomy and Posterior Gastroenterostomy*

Before the Second World War, I was satisfied that subtotal gastrectomy was the best standard treatment for duodenal ulcer, and I regarded the various discomforts and disabilities that patients suffered afterwards as the price paid for the elimination of ulcer pain and the risks of hæmorrhage and perforation, but on my return from the Services in 1946 when I read the reports of the vagotomy operations I was so impressed that in November 1947 I decided to treat all my patients with chronic duodenal ulcers by vagotomy with or without gastroenterostomy. Naturally each patient so treated was carefully assessed and individually scrutinized by myself as I was always ready to revert to gastrectomy if the results were not as good as those to which I was accustomed. It was soon obvious that vagotomy by itself, in the patient whose ulcer demanded surgery, was not sufficient and gastroenterostomy became an essential part of the operation.

Since November 1947 I have not performed a gastrectomy for chronic duodenal ulcer alone, except in massive hæmorrhage requiring emergency gastrectomy.

From November 1947 to December 1958 I performed 1,147 vagotomy operations for chronic duodenal ulcer and marginal ulcer. There were 5 deaths. All other patients left hospital alive and well.

During 1957 and 1958 we studied the first 661 consecutive vagotomy and gastroenterostomy operations in this series performed in 4 hospitals in Newcastle and Gateshead up to 1955. This survey was carried out entirely by my Registrars Mr. J. Oldfield and Dr. W. E. Suffield who examined each patient. This was a deliberate policy on my part because I believe it is difficult for the surgeon who has performed the operation

TABLE I.—INDICATION FOR OPERATION

Failed medical treatment		486
History of hæmorrhage		151
Hæmatemeses	89	
Melæna only	62	
Previous perforation		131
Symptoms of stenosis		187

TABLE II.—TYPE OF ULCER

Duodenal	622	Gastric	11
Gastroduodenal	24	Double	4

TABLE III.—COMPLICATIONS OF OPERATION

Chest complication:		Vomiting	15
Basal collapse	27	Diarrhœa	28
Simple bronchitis	43	Peritonitis	1
Pulmonary infarction	3	Ileus	10
Hæmorrhage:		Dysphagia	11
Wound	2	Other complications:	
Internal	6	Œsophagitis, venous thrombosis, etc.	20
Infection:			
Slight (wound)	16		
Serious (subphrenic)	1		

TABLE IV.—OPERATIVE DEATHS
(Total deaths in 1,147 patients: 5)

Patient	Age	Condition and operation	Post-mortem report
C. S. R. W. 1949	40	Chronic duodenal ulcer with stenosis. Old perforation. Transferred from physicians	Lower nephron necrosis. Uræmia. 3rd day
R. S. T. 1952	48	Chronic duodenal ulcer. Phthisis (inactive)	Coronary thrombosis 4th day
H. H. 1951	44	Chronic duodenal ulcer. Old perforation. Admitted in severe congestive heart failure, and big liver and œdema. Gross pyloric stenosis and persistent vomiting. Operation four weeks after admission	Mitral stenosis. Gross aortic and coronary atherosclerosis. 6th day
P. C. 1949	71	Chronic duodenal ulcer	Myocardial degeneration. 1 pint blood beneath diaphragm. 7th day
E. B. 1958	74	Chronic duodenal ulcer. Gall-stones. Myocardial ischæmia	Pulmonary collapse. Coronary thrombosis. 7th day

In the 661 patients under review 3 deaths only

TABLE V.—FOLLOW-UP (638 PATIENTS)

Good health	579		(11 had gastrectomy)
Not good health	59		(7 had gastrectomy)
Ability to work:			
Yes	551		
No	34		
No because of unrelated causes	39		
Retired	14		
Do you consider you are			
Cured?	329	622	(5 had gastrectomy)
Greatly improved?	293		(9 had gastrectomy)
Not improved?	15		(3 had gastrectomy)
Worse?	1		(1 gastrectomy)

TABLE VI.—LENGTH OF TIME SINCE OPERATION

Less than 1 year	39
1 year—1 year 11 months	51
2 years—2 years 11 months	53
3 years—3 years 11 months	68
4 years—4 years 11 months	108
Over 5 years	282
Not known	3

TABLE VII

(1) Deaths	3
(2) Stomal ulcer	6
(3) Recurrent duodenal ulcer	4
(4) Pulmonary tuberculosis	5
(5) Carcinoma	2
(6) Gastric ulcer	1
Unrelated deaths	19
Subsequent gastrectomies	18

to get factual information at a follow-up as his patients are usually so grateful to him and anxious to please that they often minimize or suppress symptoms. I do not think that postal questionnaires are nearly so satisfactory as an individual interview.

Tables I—VII show the sort of results that are being obtained in chronic duodenal ulcers treated by vagotomy and posterior gastroenterostomy. The ten-year follow-up is now being continued.

My present view is that this operation is the best treatment for all chronic duodenal ulcers requiring surgery. The operation is a safe one; it is no more difficult but may at times be more tedious than a gastrectomy. It is completely successful in a high proportion of patients, enabling them to enjoy normal meals without discomfort and without other unpleasant sequelæ of gastrectomy. If the operation is unsuccessful, perhaps due to incomplete vagotomy or some mechanical cause, a partial gastrectomy may then be performed.

Mr. Harold Burge (London):

I wish to put before you the ten-year results of vagal nerve section for chronic duodenal ulceration. The five-year and eight-year results of these series have already been published (Burge and Clark, 1959). No case has been followed for less than nine years, and the majority for ten to twelve. Table I shows the important features in the series of vagotomy with gastroenterostomy, and Table II in the series with vagotomy and pyloroplasty.

From this, it will be seen that even with an

TABLE I.—VAGOTOMY AND GASTROENTEROSTOMY: TEN-YEAR FOLLOW-UP

Total No.	301	
Lost to follow-up	11	
Dead, not from ulcer	28	
Number followed	262	
Recurrent ulcer	10	(3·8%)
Gastric ulcer	2	(0·7%)
Later operation for stenosis	1	(0·3%)

TABLE II.—VAGOTOMY AND PYLOROPLASTY: TEN-YEAR FOLLOW-UP

Total No.	140	
Lost to follow-up	7	
Dead, not from ulcer	7	
Recurrent ulcer (including gastric ulcer)	4	(3·1%)
Gastric ulcer	3	(2·3%)
Later operation for stenosis	6	(4·7%)

incomplete nerve section rate of probably 30%, the proved recurrence rate at ten years in both series is about the same, or a little greater than after subtotal gastrectomy. We may conclude that, given complete nerve section, the recurrence rate is very low. It is interesting to find ourselves believing that a properly performed vagotomy carries a lower recurrence rate than subtotal gastrectomy. The incidence of gastric ulceration at ten years after vagotomy is very low, being 0·7% in vagotomy and gastroenterostomy, but 2·3% in vagotomy and pyloroplasty. 4·7% of the pyloroplasty series came later to operation for stenosis, and usually more than five years post-operatively. It was in these cases that gastric ulceration seemed to occur. Such stenosis appears to have arisen from the faulty choice of pyloroplasty in the presence of duodenal stenosis or from the operation of pyloroplasty alone. I have no figures for the operation of pylorectomy.

I will not discuss here the test which has been described for proving complete nerve section during operation (Burge and Vane, 1958) except to say that by its use nerve section need never be incomplete.

The only disturbing feature of the operation of vagotomy with gastric drainage has been the incidence of diarrhœa with pale fatty stools. This led us to compare the incidence of diarrhœa in cases of complete vagal nerve section with selective vagotomy preserving the cœliac division of the posterior nerve. From our studies, we have concluded that the preservation of this nerve is important and indeed an essential part of vagotomy.

We must conclude that if our ten-year figures are true, and clearly they are, and if incomplete nerve section need never be done, and it need not, and if post-vagotomy diarrhœa can be prevented, and we think it can, then no case can be made out for subtotal gastrectomy for chronic duodenal ulceration.

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Mr. Norman C. Tanner (London):

There is a tendency, particularly in ulcer surgery, to vary one's opinions on the treatment according to the well-being or otherwise of the last patient seen. I have vagotomized and gastrectomized patients who serve petrol at different garages around my hospital. They are fortunately all very well and when I reach hospital after a "fill-up" I have an emotional desire to treat that day's cases with the same operation that I had used on the last petrol attendant I saw. Such methods, I am afraid, are unscientific and we must revert to making up our minds on the combination of a late follow-up of cases, with an overall mental assessment of the operation.

How can we decide between two operations even after a follow-up? If we compare the state of well-being of our successes, then undoubtedly the most successful is simple gastrojejunostomy, but this operation is indefensible because of the high stomal ulceration rate. In a ten-year follow-up of 126 cases, we had a 50% stomal ulcer rate. There is not much to choose between the state of well-being of a successful vagotomy and a successful gastrectomy. Perhaps the former have a heavier average weight, but the return to what the late Dr. Arthur Allen called the "college weight" of some gastrectomies may be cardiologically beneficial. Comparing the persistent duodenal or the stomal ulceration rate, gastrectomy has an advantage over vagotomy. What about the bad results not due to recurrent ulcer? In both series lie those badly selected for surgery, and there is little to choose between them. There is little to choose between troublesome diarrhœa and severe dumping, but fortunately both in our experience are unusual.

Tables I and II give the results of a follow-up of cases operated on by many surgeons—consultants, registrars and certain senior house surgeons at St. James' Hospital. These figures were worked out by Dr. Brian Swynnerton (vagotomy results) and Mr. A. M. Desmond (gastrectomy results).

TABLE I.—OPERATIVE MORTALITY
(All Hospital Cases)

To end of 1957	No.	Deaths	Mortality rate
Vagotomy and pyloroplasty ..	226	1	0·4%
Vagotomy and gastrojejunostomy	134	4	3·0%
Consecutive cold gastrectomies ..	643	14	2·2%

TABLE II.—COMPARISON BETWEEN THE LATE RESULTS OF VAGOTOMY AND GASTRECTOMY

Grade (Visick)	Vagotomy and pyloroplasty	Vagotomy and gastrojejunostomy	Gastrectomy
1	42·1%	54·0%	68·3%
2	25·2%	18·0%	16·1%
3 (S)	15·7%	14·0%	7·8%
3 (U)	8·2%	4·0%	
4	8·8% (1·5%)	10·0% (5·6%)	7·8% (1·3%)
Total No.	159	50	322

NOTE.—The gastrectomy results were on a lower % follow-up of those operated on than the vagotomies. The figures in brackets are the persistent or recurrent ulcer figures.

From these figures, gastrectomy would still seem to be a very satisfactory operation.

I carried out my first partial vagotomy in 1943. In 1947, we began to combine complete vagotomy with pyloroplasty and in 1948 the addition of a pyloroplasty became routine. We did, however, add a gestrojejunostomy to some cases and a follow-up in 1955 showed that the results of vagotomy combined with gastrojejunostomy were on the average superior to those obtained by its combination with pyloroplasty, except for the slightly greater technical difficulty of dealing with a gastrojejunal ulcer rather than a persistent duodenal ulcer. In 1940–43, I began to employ what I called an anterior juxta-pyloric gastrojejunostomy for duodenal ulcer (Tanner, 1946) and in 1953 we made a ten- to twelve-year follow-up. A ten-year follow-up showed for orthodox posterior gastrojejunostomy a 50% stomal ulcer rate, for posterior juxta-pyloric gastrojejunostomy a 64% stomal ulcer rate and for anterior juxta-pyloric gastrojejunostomy a 26% stomal ulcer rate. The anterior juxta-pyloric operation is the easiest of the three to do and, perhaps just as important, it is easy to undo. In 1953, therefore, we began to combine vagotomy with our most successful long-term form of gastrojejunostomy and that is the combination we now use.

Finally, let me add one or two recommendations. I believe vagotomy is desirable for the patient with active or quiescent pulmonary tuberculosis, or for a patient who is grossly underweight for some non-ulcer cause. It is also reasonable to use when each ulcer breakdown is preceded by a definite period of anxiety. I use it in children under 20 years of age unless there is stenosis. Gastrectomy should be used if there is any gastric obstruction, if there is a recent hæmorrhage, or if there is the slightest suspicion of gastric ulcer or even of previous gastric ulcer scarring.

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Mr. C. W. A. Falconer (Edinburgh):

I would like to present some data from the Gastro-Intestinal Unit of the Western General Hospital, Edinburgh, and to indicate how they may influence the surgeon in the choice of operation for duodenal ulcer.

For some five years the "maximal" histamine response (Card *et al.*, 1955) has been used as a measure of the potential acid output of the stomach, and it has been found to be a useful guide to the selection of the correct procedure for each individual patient with duodenal ulcer.

TABLE I.—SECRETORY RESPONSE TO "MAXIMAL" HISTAMINE STIMULATION

Group	No. of subjects	Basal secretion mEq.HCl		Maximal secretion mEq.HCl	
		Mean	Range	Mean	Range
Normal males	14	2·5	0·9·5	22·4	10·1–34·6
Normal females	18	1·3	0·6·8	14·6	0·1–31·3
Duodenal ulcer (uncomplicated):					
males	176	6·0	0·1–23·1	37·5	4·2–91·7
females	61	3·2	0·1–14·9	24·3	4·6–43·9
Post-operative dyspepsias:					
(*a*) Recurrent gastric and suture line ulcers	9	1·4	0·15–4·2	4·3	0·8–14·7
(*b*) Jejunal ulcers					
following gastroenterostomy	10	8·7	5·1–30·0	43·5	26·8–60·7
following gastrectomy	14	7·7	0·6–19·8	31·1	7·7–82·0
(*c*) Dyspepsia, but no ulcer	8	1·5	0·1–4·0	4·7	0·3–11·3

From Bruce *et al.* (1959). By kind permission.

Table I illustrates the range of values obtained by this test in normal subjects, patients with duodenal ulcer, and patients with recurrent ulceration. It shows that in duodenal ulceration the mean acid output is nearly double that of the normal stomach, and individual cases may show much higher levels of secretion than the mean. It also shows that in the case of jejunal ulceration following gastroenterostomy or gastrectomy, the operation has not reduced the acid output to anything like normal.

In 4 patients from the Gastro-Intestinal Unit who developed jejunal ulcer after gastrectomy, the pre-operative acid secretion was so high that a standard gastrectomy failed in its purpose and the post-operative acid output remained well up in the ulcer-provoking range, and jejunal ulceration followed within two years (Table II).

TABLE II.—ACID OUTPUTS BEFORE AND AFTER GASTRECTOMY IN FOUR SUBJECTS DEVELOPING JEJUNAL ULCER

Pre-operative levels in mEq.		Post-operative levels in mEq.		Post-operative interval before jejunal ulcer appeared
Basal	Maximum	Basal	Maximum	
23·1	91·7	9·6	38·2	3 months
4·2	48·5	2·0	16·7	12 months
10·8	73·0	3·1	28·2	24 months
21·0	75·0	7·0	27·0	6 months

From Bruce *et al.* (1959). By kind permission.

Vagotomy will reduce the acid secretion of the stomach by two-thirds to three-quarters. The reduction affects both the basal acid secretion and the response to histamine stimulation. The reason for the latter effect is not fully understood but it may be related to altered blood flow.

Table III shows the correlation between the level of acid secretion in response to histamine stimulation and in response to insulin-induced hypoglycæmia before and after vagotomy and gastroenterostomy. The mean reduction achieved amounts to 70·8% in relation to "maximal" histamine stimulation and 76·1% with the insulin test, and a vagotomy may be said to reduce the acid output by over two-thirds. A standard gastrectomy, removing about two-thirds of the stomach, will also reduce the acid secretion by about two-thirds, and it can be seen that in this group of patients the majority would have been protected by either procedure, and the choice of operation is a matter of personal preference.

It is in the group of high secretors that these operations may fail, and we take the figure of 50 mEq. HCl in the first post-histamine hour as the level above which jejunal ulcer is likely to occur. For these patients we prefer to reinforce a standard gastrectomy by the addition of vagotomy, and so reduce the acid output by up to 90% of the pre-operative level. The last patient (014295) in Table III is in this group. A vagotomy and gastrectomy was indicated but owing to serious hæmorrhage from the inferior phrenic vein during the vagotomy, a gastroenterostomy was made in preference to gastrectomy, to shorten the duration of the operation. It is anticipated that a jejunal ulcer may develop sooner rather than later.

In the Gastro-Intestinal Unit it is our practice to use gastroenterostomy alone in some elderly pyloric stenotics, and vagotomy and gastro-

TABLE III.—VAGOTOMY AND GASTROENTEROSTOMY. COMPARISON OF SECRETORY RESPONSE TO "MAXIMAL" HISTAMINE STIMULATION AND TO INSULIN-INDUCED HYPOGLYCÆMIA, BEFORE AND AFTER VAGOTOMY AND GASTROENTEROSTOMY

Case No.	Sex	"Maximal" histamine stimulation			Insulin-induced hypoglycaemia		
		Acid output (mEq./hr.)		Reduction %	Max. output (mEq./hr.)		Reduction %
		Pre-op.	Post-op.		Pre-op.	Post-op.	
016477	F	30·8	8·0	74·0	15·0	4·0	73·3
013336	F	34·0	3·3	90·3	18·1	0·5	97·6
017182	F	19·5	7·2	63·1	6·5	2·2	66·1
016386	M	30·0	18·6	38·0	28·8	9·1	68·4
06665	F	27·0	2·0	95·9	5·6	0·2	96·4
014295	M	57·7	21·2	63·2	33·6	13·1	61·0
Means		33·1	10·0	70·8	17·9	4·8	76·1

enterostomy for women, youths, and adult or elderly males in whom other factors weigh against gastrectomy. We still believe that gastrectomy is the best operation for the average male, with a moderately high acid output, while in the high secretion group, over 50 mEq./hr., a standard gastrectomy reinforced by a vagotomy is preferred to an excessively high gastrectomy. While the mortality from vagotomy and gastroenterostomy is low, the diarrhœa which may follow it, and which is not invariably relieved by sublingual Mechothane, is of sufficient frequency to be considered a disability when comparing this operation with gastrectomy. It is comforting, however, to know that the acid reduction obtained by vagotomy and gastroenterostomy is comparable with that achieved by gastrectomy, and that the angry inflamed duodenum, or the chronic penetrating ulcer, need no longer be a challenge to the intrepid surgeon: a vagotomy and gastroenterostomy will do all that the gastrectomy would have done without the risks associated with a difficult duodenal dissection. Should a jejunal ulcer appear later, and a gastrectomy be required, the duodenum would be found to be quiescent and the operation relatively straightforward.

REFERENCES

BRUCE, J., CARD, W. I., MARKS, I. N., and SIRCUS, W. (1959) *J.R. Coll. Surg., Edinb.*, **4**, 85.
CARD, W. I., MARKS, I. N., and SIRCUS, W. (1955) *J. Physiol.*, **130**, 18P.

Professor R. B. Welbourn (Belfast):

I wish to draw attention to a type of peptic ulceration in which conventional gastric surgery is often useless. I refer to the Zollinger-Ellison syndrome, which Dr. Dragstedt has already mentioned. This consists of (1) a fulminating peptic ulcer diathesis; (2) gross gastric hypersecretion (2 to 6 litres of highly acid juice in twelve hours); and (3) a tumour or tumours of the pancreatic islet cells which do not secrete insulin. The syndrome is rare, but since it was described four years ago many examples of it have been recognized.

The ulcers are often multiple and in unusual sites. Many of them are below the ampulla of Vater and some in the jejunum. They are very liable to serious complications and they recur rapidly after normally adequate surgery. Many patients have had numerous operations and most have died from the complications of peptic ulcer.

The gastric juice is rich in pepsin, suggesting a vagal origin, but the hypersecretion persists in an astonishing way after complete vagotomy, even when it is combined with high gastrectomy. When the tumours are well differentiated the alpha cells of the islets, which can be recognized by special staining, predominate.

The treatment which Dr. Zollinger recommends for the ulcer is a total gastrectomy. This policy has been followed in several cases recently with striking success. It is possible that the tumours in some way cause the hypersecretion and the ulceration, for a few cases are on record in which removal of the tumour has cured the ulceration after several operations on the stomach have failed to do so. It seems reasonable, therefore, to do a subtotal gastrectomy and vagotomy (instead of a total resection) if, and only if, it is reasonably certain that all the tumour tissue has been removed.

REFERENCE

ZOLLINGER, R. M., and ELLISON, E. H. (1955) *Ann. Surg.*, **142**, 709.

Professor Andrew W. Kay (Sheffield):

In attempting to assess a surgical procedure in the treatment of duodenal ulcer, it is difficult to exclude an element of bias. The first point I wish to make concerns a method of trial which permits an unprejudiced assessment of the value of various surgical procedures.

In 1955, in Professor C. F. W. Illingworth's Unit in the Western Infirmary, Glasgow, we decided to institute a controlled trial in which male patients aged 20 to 65 years with uncomplicated duodenal ulcer were treated by one of three procedures—gastrojejunostomy, gastrojejunostomy with vagotomy, and partial gastrectomy. At operation, unless gastrectomy or vagotomy was precluded for technical reasons, the particular operation to be done was determined by random selection. There were 20 patients in each group; the groups did not differ significantly in respect of age, duration of ulcer symptoms or pre-operative maximal acid output as judged by the augmented histamine test.

Vagotomy was performed by the abdominal route; gastrectomy was of the Polyă type and posterior gastrojejunostomy was made with a short isoperistaltic loop and a small stoma close to the greater curvature at its most dependent point. There were no operative deaths and no significant difference in the duration of stay in hospital following operation. All patients have been seen at three months, six months, one year, two years and three years after operation and graded according to the severity of their post-operative symptoms by an observer who was unaware of the operation performed (Table I). The results of the three-year follow-up are shown in Table II.

3 patients have died, the cause of death in each case being unconnected with ulcer disease; one patient emigrated and was well when last seen two years ago. If Groups III and IV are taken together (patients with troublesome symptoms and those regarded as complete failures) it

TABLE I.—METHOD OF GRADING USED TO ASSESS POST-OPERATIVE RESULTS

Result	Grade
Good result	I
Minor symptoms (not causing inconvenience)	II
Moderate symptoms (patient and observer satisfied that there has been improvement as compared with pre-operative ulcer distress)	III
Poor result	IV

TABLE II.—THREE-YEAR FOLLOW-UP OF 60 MALE PATIENTS WITH DUODENAL ULCER TREATED BY GASTRO-JEJUNOSTOMY, GASTROJEJUNOSTOMY AND VAGOTOMY, OR PARTIAL GASTRECTOMY

Grade	Gastro-jejunostomy	Gastro-jejunostomy + vagotomy	Partial gastrectomy
Dead or untraced*	1	2	1
I	11	12	12
II	2	4	6
III	1	0	1
IV	5	2	0

*These 4 patients were Grade I at their last attendance.

will be seen that 6 had bad results after gastro-jejunostomy, whereas only 2 had poor results from gastrojejunostomy plus vagotomy, and 1 from gastrectomy.

The results of this pilot study confirm the growing belief that gastrojejunostomy alone has no longer a place in the routine management of patients with duodenal ulcer. It appears, however, that the addition of vagotomy protects the gastrojejunostomy stoma and a large trial comparing the results of vagotomy with those of partial gastrectomy has since been undertaken in Glasgow using similar random methods of selection and follow-up.

While it is desirable that the available procedures be evaluated by some such method as I have indicated, this approach seems to be based on the assumption that a single procedure will prove eventually to be the most effective one for *all* patients with duodenal ulcer. Perhaps more attention should be paid to the objective of selecting the operation for the individual case. In support of this view I offer some preliminary results for which I am indebted to my former assistant (Mr. James McArthur) and my present assistant (Mr. Iain Gillespie), who have been responsible for this investigation.

It is well known that vagotomy reduces the gastric acid output as measured by the spontaneous secretion, the nocturnal secretion and the response to small doses of histamine. The precise reduction in acidity has been difficult to determine since none of these tests can be relied upon to give consistent results when repeated in normal subjects. Reproducibility is, however, one of the main advantages of the augmented histamine test and we have now applied this test before and after vagotomy with gastro-jejunostomy to over 50 patients. We have found that, while the majority of patients have a reduction in maximal acid output of well over 50%, a proportion (approximately 15%) have a reduction of considerably less than 50%. It could of course be argued that in this small group of patients vagotomy was incomplete, and it is now our practice in Sheffield not only to perform the augmented histamine test but to note also the influence of medical vagotomy on this response before operation. Satisfactory medical blockade can be achieved by giving hexamethonium and atropine in combination by intramuscular injection (Fig. 1). In this way

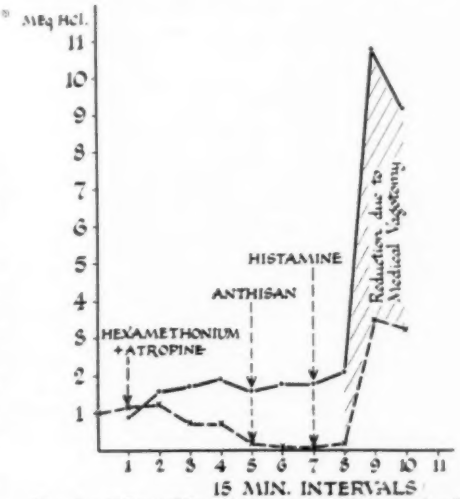

FIG. 1.—Effect of "medical vagotomy" on maximal histamine acid output. The continuous line represents the response to the augmented histamine test in a patient with duodenal ulcer; the broken line shows the reduction in this response from previous administration of hexamethonium (50 mg.) and atropine (0·325 mg.).

we have been able to show that patients having a poor reduction in maximum acid output to medical vagotomy will also have a poor response to surgical vagotomy (Table III).

TABLE III.—COMPARISON OF MEDICAL AND SURGICAL VAGOTOMY ON THE AUGMENTED HISTAMINE RESPONSE

Patient	Percentage reduction in maximum acid output	
	Medical vagotomy	Surgical vagotomy
1	21·4	29·3
2	15·5	20·1
3	17·3	32·0

It is fully appreciated that these tests provide a physiological assessment of the operation only, and we await the clinical follow-up of vagotomy in such patients with great interest since it seems to us that they would have been managed more correctly by partial gastrectomy.

I would like to express my thanks to Mr. A. P. M. Forrest of the Department of Surgery, Glasgow University, for providing me with the most recent follow-up results of the controlled trial and also to Mr. James McArthur who will shortly publish his paper comparing medical blockade and surgical vagotomy on maximal gastric acid secretion.

Mr. R. H. Franklin (London):

On the whole the results of partial gastrectomy for duodenal ulcer are satisfactory. Some of the so-called postgastrectomy symptoms are due to the patient trying to eat too large a meal before the stomach has had time to become adapted to the results of the operation. Failure to gain weight is sometimes due to the fact that the patient was overweight before the operation. It is, of course, recognized that occasionally a patient will become extremely thin as a result of the gastrectomy and this may be a handicap, particularly in a patient who is doing hard physical work.

There are one or two complications of vagotomy which have not been referred to. Occasionally a hiatus hernia develops following an abdominal vagotomy. Symptoms of this may ultimately prove to be more severe than the symptoms of the original duodenal ulcer. Damage to the œsophagus can also occur.

Reference has been made to the possibility of carrying out a partial gastrectomy at a later date should the vagotomy not prove satisfactory. The difficulty about this, apart from the undesirability of carrying out two operations unless it is absolutely necessary, is that the gastrectomy may be extremely difficult owing to the adhesions which may form as the result of the vagotomy. When dealing with patients of middle age in whom one expects a good result from a partial gastrectomy, my own preference is to carry out a partial gastrectomy in the first instance and to resort to a transthoracic vagotomy in the few patients who develop a jejunal ulcer. The procedure of vagotomy, together with pyloroplasty or some other form of drainage operation on the stomach, should be reserved for the following patients: (1) Very young patients who have failed to respond to a medical regime; (2) Cases in which the duodenal ulcer involves a "dangerous" part of the duodenum where resection might involve risk of damage to the bile ducts or present extreme difficulty in closure of the duodenal stump; (3) Patients at the other end of the scale in whom the ulcer is so small that it is difficult to justify carrying out a partial gastrectomy.

Professor C. A. Wells (Liverpool):

I am surprised that so much emphasis has been laid by previous speakers upon the incidence of stomal ulcer which I regard as largely a thing of the past. However, if surgeons continue to practise gastroenterostomy and Billroth I procedures in duodenal ulcer, they must expect to get the same incidence of this complication as was noted by earlier operators fifteen, twenty and more years ago. In particular, I would condemn simple gastrojejunostomy in pyloric stenosis; the fact of there being stenosis is ample proof of the activity of the ulceration and a sure promise that when stasis is relieved hyperacidity will return. Such cases are amongst those most likely to lead to stomal ulceration. Gastrectomy or short circuit with vagotomy is the procedure called for.

In my own modification of the Billroth I procedure, after vagotomy, a wide stoma is made between the remaining stomach and the duodenum, without disturbance of the ulcer. The operation has the virtue of safety. It has, however, been disappointing to find after 100 hemigastrectomies with vagotomy and this type of anastomosis that dumping, although only half as frequent as in a similar series of Polya operations, is still troublesome. By limiting the resection to the pyloric antrum it promises to be possible to reduce the incidence of this complication still further. We are currently running, by random choice, a fully controlled comparison between gastroenterostomy and gastroduodenostomy, with vagotomy in both cases, but it is too early to report. There seems much to be said for tests of this character as the only reliable way of detecting minor differences between the results of two permissible and nearly comparable procedures.

The third point I wish to make is that the result of a good operation may be spoilt by gastro-œsophageal reflux if hiatal hernia is not excluded at the time of operation or if it is produced by clumsy performance of vagotomy by the abdominal route. After this procedure the normal gastro-œsophageal angle should always be restored and the hiatus sutured if necessary. Coincident duodenal ulcer and hiatus hernia may, with advantage, be treated by vagotomy, antrectomy and ante-colic Roux anastomosis in Y (Wells and Johnston, 1955).

Finally, in stomal ulceration following any procedure, if the stoma is working well the best operation is usually vagotomy by the thoracic route. This is a safe and simple procedure in which the operator is not tempted to carry out further surgery on the stomach which can easily land him and his patient in grave trouble.

REFERENCE.—WELLS, C. A., and JOHNSTON, J. H. (1955) *Lancet*, i, 937.

Professor F. A. R. Stammers (Birmingham):

Between 1946 and 1953 the three surgeons of the Surgical Professorial Unit in Birmingham performed partial gastrectomy on 955 patients for chronic peptic ulcer. Excluding cases of combined gastric and duodenal ulcer, of stomal ulcer, and patients who would not attend for follow-up beyond a year, there remained 749 cases, of which 485 were duodenal ulcers, comprising 403 men and 82 women.

In 1956 Thorn and Brookes analysed the whole group of 955 cases, with particular reference to any possible relationship between the development of tuberculosis and the operation of gastrectomy, at the same time collecting sufficient information and details for an analysis of results regarding dyspepsia in relation to the type of operation performed. This latter information has guided us in our subsequent choice of surgical treatment of duodenal ulcer, and Mr. Brookes, together with Dr. J. A. H. Waterhouse of the Department of Medical Statistics in Birmingham, is about to publish this detailed analysis. The patients are still being followed up, and so, too, of course, are those operated on since 1953.

In round figures over-all results of these 485 cases were much the same as those of other centres, namely:

Mortality rate <4%. 1·8% under the age of 50 years. 14% over the age of 65 years.

Cured, 68%: Those really free from dyspepsia, or so improved as to be able to live a full life.

Much improved, 16·5%: Those so much better than before that they can work fully, but still have to restrict themselves in diet.

Failed, 11·5%: About half of these have never been satisfactory from the beginning: the other half developed dyspepsia again after several years of good health.

Brookes and Waterhouse have taken the following points into consideration: (1) Polya *versus* Billroth I. (2) Major resection *versus* minor resection, i.e. more than or less than two-thirds of the stomach removed. Thus:

Polya	2/3 resection or less—	males 277, giving 71% successes. females 61, giving 57% successes.
	Over 2/3 resection —	males 92, giving 61% successes. females 15, giving 53% successes.
Billroth	2/3 resection or less—	males 26, giving 65% successes. females 6, giving 65% successes.
	Over 2/3 resection —	males 8, giving 87% successes. females 0.

They also enquired into any significant differences between antecolic and retrocolic reconstruction and between using a valve or no valve, and concluded as follows:

(1) For duodenal ulcer there is no difference between the Polya and Billroth I operations. (For gastric ulcer, the Billroth I operation gave significantly better results.)

(2) In men, the more limited resections gave better results, whether Polya or Billroth I.

(3) In women, the antecolic type of reconstruction gave significantly better results than the retrocolic operation.

(4) Valves had no advantages in the Polya operation for duodenal ulcer.

Based on these facts, and as a result of a study of failed cases, my general views are now as follows:

(1) It is essential to be sure of the patient's psychological stability before deciding on operation.

(2) Apart from complications, it is better not to operate too early after the development of dyspepsia. The patient should learn by experience what a duodenal ulcer really means to him before he is offered surgical treatment, which itself might leave minor discomforts. I think two years is about right.

(3) In patients aged about 45 years or more, I resect no more than two-thirds of the stomach, and more often only half, and then add an infradiaphragmatic vagotomy. The dumping syndrome, though sometimes due to subtle metabolic factors, is commoner after major resections, i.e. those leaving a small reservoir.

In young patients (under 30 years), I perform vagotomy and a retrocolic gastroenterostomy to the antrum, using that part of the jejunum that lies against it: this means a loop of no more than 1 or 2 in. (2·5 or 5 cm.), sometimes none.

(4) In tuberculous patients of any age, in whom it is important not to lose weight, a vagotomy and gastroenterostomy are used.

(5) In the antecolic operation, the loop should not exceed 4 in. (10 cm.). The gap between the anastomosis in front and the transverse colon behind should be closed with stitches.

(6) In retrocolic partial gastrectomy there should be no loop.

(7) In any of the techniques the stomach and jejunum should be joined together in such a way that there are no twists, kinks or redundant loops.

REFERENCE

THORN, P. A., and BROOKES, V. S. (1956) *Brit. med. J.*, i, 603.

Mr. G. E. Moloney (Oxford):

A series of 103 Billroth I operations with approximately two-thirds resection produced better functional results than my Polya operations for duodenal ulcer. But a high recurrence rate of 7% induced me, in 1951, to add vagotomy to the Billroth I procedure and to reduce the resection to hemigastrectomy, and a little later

to reduce it still further to antrectomy only, hoping by these two measures to prevent both recurrent ulceration and the small stomach syndrome. These objects appear to have been achieved. I have now performed vagotomy and antrectomy with gastroduodenal anastomosis over 200 times (all followed-up with four exceptions) with 100 operated on more than four years previously and with no recurrences revealed on follow-up. The capacity for food is much better with gastric resection limited to antrectomy, and after two years almost all patients make no complaints about capacity. Weights are well maintained and, after six months, fluctuation appeared to be independent of the operation. Dumpers are rare being only two, one mild and the other moderate. Bile vomiting, a symptom found by Mr. R. L. Holt to be troublesome with gastroenterostomy and vagotomy, occurred in the recumbent position in two patients who were found to have small hiatus weaknesses, and also slightly in two others of the 100 patients operated on four years previously. Bowel function after vagotomy has been criticized from the aspect of looseness, though no one has commented that some patients become constipated. Analysis of bowel function in the 100 patients operated on more than four years previously is as follows:

TABLE I.—BOWEL FUNCTION IN 100 PATIENTS WITH OPERATION FOUR YEARS PREVIOUSLY

Bowel function changed ..	41
Easier, but once a day only	37
Become constipated (motion hardened or two days or more)	11
Occasional looseness or diarrhœa	11

TABLE II.—ANALYSIS OF THE SYMPTOMS IN PATIENTS WITH ANY COMPLAINT OF LOOSE BOWEL FUNCTION

Occasional looseness (1, 2 or 3 motions a day) ..	5
Loose action one hour after normal one ..	1
Normal for a week, loose for a day, constipated for a day, then normal for a week	1
A loose action for one day in four to six weeks ..	2
A loose action for one day in three to four months	1
Diarrhœa five times daily since dysentery in Jap. P.O.W. Camp	1

Several patients are grateful for losing their constipation as well as their duodenal ulceration. Many people who have never had duodenal ulceration are much the same as these patients in respect of their bowel function. Achlorhydria, which occurs in 4% of the population and is responsible for the loose bowel actions in some people, is the probable cause of this symptom when it follows gastric surgery. If any blind loops remain such as the duodenum after gastroenterostomy or the Polya operation, loose bowel actions are liable to be worsened. The patients' opinions of their results in those 100 who had had the operation more than four years previously were excellent in 80% and good in 20%.

How dangerous is the dissection of duodenal ulcers? My experience in round figures is of over 300 resections with gastroduodenal anastomosis (100 Billroth I procedures and 200 antrectomy and vagotomy with gastroduodenal anastomosis) and these include all my operations for acute hæmatemesis and melæna. The only patient of these 300 whose death could be attributed to the dissection of his ulcer developed acute hæmorrhagic pancreatitis after a large ulcer penetrating deeply into the pancreas had been resected. Since 1951 I have found it advisable to perform only eight Polya operations because of the position of the ulcer or the build of the patients. Nowadays for particularly difficult duodenal ulcers or for distal ones near the bile duct papilla I would prefer to do gastroenterostomy and vagotomy and see how things go. But, for most duodenal ulcers, dissection and freeing of the ulcer is not difficult and the subsequent gastroduodenal anastomosis gives the most complete form of pyloroplasty, the whole pylorus going and not just the anterior portion as some advocate. It is not necessary to dissect far beyond the ulcer and if there is enough to close as in the Polya operation there is enough to anastomose as a gastroduodenostomy, and with a small gastric resection there is plenty of stomach to make ends meet without any tension on the anastomosis.

The main points in favour of this are: concomitant ulceration which occurs in 10–20% of patients is dealt with by this operation which also gives almost complete immunity from recurrent gastric or duodenal ulceration; bile vomiting and dumping are less than with gastroenterostomy and vagotomy or the Polya operation; if the duodenum is markedly distorted it is easier and better to resect the ulcer and to make a fresh anastomosis of the lumen than to attempt a difficult pyloroplasty; resection would appear the best way to secure a bleeding ulcer; leakage at an end-to-end anastomosis is less dangerous and can be treated by aspiration as with perforated duodenal ulceration, whereas leakage of a duodenal stump is likely to occur freely into the peritoneal cavity and is not influenced by gastric aspiration; no blind loops remain with the passage of food through the duodenum, and digestion and fat absorption are aided by the proper mixing of the bile and pancreatic juices with the food.

Professor H. W. Rodgers, Mr. W. M. Capper and **Mr. A. Dickson Wright** also took part in the Discussion.

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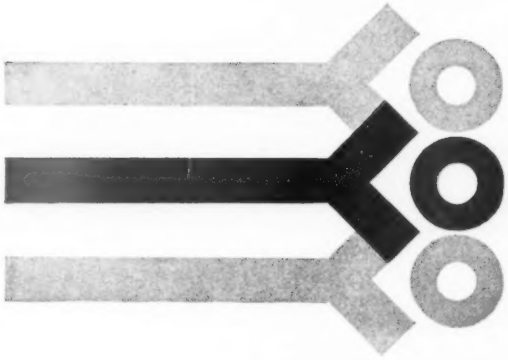

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Meeting
March 19, 1959

Melanosis of Face from "Cutting" Oil.—R. P. WARIN, M.D.

Mr. J. D. H., aged 23. Turner in aircraft industry.

History.—Six months increasing brown colour of face. Started following a few days' sun-bathing. Turner on lathe in aero-engine factory for past six years: has been on the same machine for past two and a half years. No difference in job prior to onset. Cutting oil used on machine and fine spray from this is in contact with clothing and exposed areas of skin.

Clinical findings.—Pigmentation over forehead, cheeks and chin. Slight scaling and follicular eruption on forearms and a little on the front of thighs.

Comment.—The cutting oils used are Hocut, G (a petroleum sulphonated/resin soap mixture with mineral oil) and Solcut X 6 (a mixture of potassium sulphonates and naphthenates with mineral oil). The oils have in addition germicides, coupling agents, stabilizers, deodorants, inhibitors and anti-rust additives, amongst which is 3–4% cresol. It is also well known that cutting oils readily become contaminated with lubricating oil, abrasive and metal dust.

Rook (1950) showed at a meeting of this Section a patient who developed melanosis on the forearms and forehead. The condition followed a period of sun-bathing. As an inspector of metal parts, his forearms were covered with cutting oil and he had a habit of wiping his forehead with his oily forearms.

REFERENCE

ROOK, A. (1950) *Brit. J. Derm.*, **63**, 159.

Creosote Melanosis with Associated Vitiligo and Depigmentation Due to Monobenzyl-hydroquinone.—P. HALL-SMITH, M.D., M.R.C.P.

Mr. A. M., aged 46. Carpenter.

Since the summer of 1956 he had marked pigmentation and mottled appearance of the forehead, face and arms; there were also noted areas of true vitiligo of chest wall beneath the axillæ. When first seen it was thought that he was of Indian ancestry. However, he states that both parents are British of European stock, though his mother is very dark.

He is employed as a carpenter by British Railways and has close contact with creosoted timbers; much of his work is in the open and his pigmentation increases during the summer months. He has been instructed to change his occupation and keep away from creosote, but this is apparently impossible. Owing to the fact that the patient was greatly worried about his appearance he was given some 10% monobenzyl-hydroquinone in emulsifying ointment to rub into his forehead. However, he used this preparation more widely than was intended and continued with it for twelve months until May 1958.

In the summer of 1958 it was noticed that more definite depigmented patches had developed on his arms and face. By then the monobenzyl-hydroquinone ointment had been discontinued. Although nine months have elapsed there is no sign of repigmentation taking place. In addition to this ointment he was also given 15% para-aminobenzoic acid in emulsifying ointment to use as a sun-screening agent.

Dr. A. J. E. Barlow: I would not have felt that the melanosis in Dr. Warin's case should be classed as secondary to contact with oil. This man had worked only in soluble cutting oil in which his hands were continually immersed. Water-mixed oils usually produce eczematous reactions but his hands and forearms show no significant changes. We see a large number of patients who do this type of work but I cannot recollect having seen any pigmented changes before.

Dr. F. F. Hellier: This man was the only worker in the place to get pigmentation of the skin though others were doing exactly the same job as he was. There is obviously a personal idiosyncrasy which predisposes a man to react in this way. On the other hand I have seen men in other industries, in particular making briquettes, in which almost every worker is pigmented. Here the external factor seems to be so intense that it overrides any personal idiosyncrasy.

Dr. G. Hodgson: I think the first case is a true oil effect. It is possible to get pigmentation from the less well-refined products of the higher petroleum range of distillation of crude petroleum oil, but more commonly from the lower fractions of distillation, the heavier oils and the tarry residues.

Both these men show on the backs of the hands and forearms a keratotic blocking of the follicles which suggests that the lower distillation products would be responsible, if any. It is much more common to get oil acne with the insoluble cutting oils than with the soluble cutting oils. Taking into consideration the pigmentation and the hyperplastic effect in the follicles I should have thought that this was related to the cutting oils.

Dr. H. R. Vickers: I agree with regard to the idiosyncrasy of these people. The second patient told me that every new man who goes on the job has

blistering on the face in the first summer. People who handle creosote are very light sensitive. I saw last summer a whole group of children who had been creosoting a fence and who developed a light-sensitive dermatitis.

Angio-endothelioma.—STEPHEN GOLD, M.D.

Mr. E. B., aged 74, had noticed some discoloration of the nose for six months before coming to hospital. The condition caused no symptoms and appeared as a soft, infiltrated plaque of uniform consistency overriding the bridge of the nose. The colour was a dusky brown, like leather; the border was purpuric. The epithelium was intact and there was no scaling or atrophy. Diagnoses considered were some form of lymphoma, granuloma faciei, sarcoidosis or an unusual variant of lupus erythematosus. The first biopsy did not throw light on its identification though a subsequent review of this earlier slide did show suspicious changes. In fact the patient was observed for three more months during which time the plaque became larger and more fleshy. A second biopsy was reported as follows (St. George's Hospital): "There is an infiltration of the dermis by an endotheliomatous lesion composed of irregular spaces lined by large cells with hyperchromatic nuclei. Some of these cells show nuclear pleomorphism and there are a few mitoses. There are some intraluminal papillary projections as well as a moderate lymphocytic infiltration. The appearances are those of an endothelioma with features suggesting malignancy." The substance of this report was confirmed by Dr. H. Haber.

Treatment.—Surgical excision of the area with a two-millimetre margin extending to the bony and cartilaginous structures of the nose was carried out on 27.8.58 by Mr. Elliot Blake, the defect being replaced by a hairless Thiersch graft. Healing was satisfactory but subsequent pathological examination revealed that the excision had not been complete. Within six months it became clinically apparent that this was so with the appearance of a small purple nodule in the lower pole of the grafted area.

POSTSCRIPT.—Further surgical excision was attempted in June 1959 but once more the lines of excision have not cleared the infiltrate. The patient remains well and there is no adenopathy. High voltage X-irradiation is now being given.

"Neurotrophic Atrophy."—J. SCHNEEWEISS, M.B. (for S. C. GOLD, M.D., F.R.C.P.).

Mr. S. H., aged 55. Optical frame maker.

History.—Presented in Dermatology Department of Hammersmith Hospital on 13.5.58 with extensive ulcerations of both legs. Through the co-operation of other hospitals, his history can be followed accurately back to 1926 when he spent six months in St. Bartholomew's Hospital for treatment of "chronic ulceration of legs".

When first seen there, he gave a three-year history of the development of a "corn" on the plantar surface of the left great toe. He employed a safety-razor to "pare" this lesion, which spread farther each time till it became the size of a half-crown. Ankle swelling then ensued, and the left leg became "itchy", leading to self-treatment with dry lint and warm water. Nine months before admission ulcerations developed and involved both legs. His skin was brown and indurated and the several ulcers present were described as being shallow, with sloping edges and a granulating base. His Wassermann reaction was negative and X-rays of his legs showed the bones to be thickened and irregular. He responded well to treatment with potassium iodide, liquid paraffin and eusol, and lotio rubra.

The patient continued self-treatment throughout the years, progressive shrinkage of both feet taking place. In 1944 he was "bombed-out" and was admitted to another hospital, where he remained for five months. He was considered to be suffering from chronic osteomyelitis and was treated accordingly. Amputation was advised, but the patient refused this.

When first seen in May 1958 his ulcers had recently become more troublesome, his left leg, where they extended beyond the knee, being more severely affected than the right. He was treated with local applications and his skin improved. His admission for further investigations was arranged (Fig. 1).

FIG. 1.—Appearance of leg after initial treatment.

Family history.—One brother, who died in 1948 following a severe hæmatemesis due to duodenal ulceration, had had a mid-thigh amputation of his left leg in 1937. He had given a similar history of recurrent ulcerations and his bone X-rays showed changes similar to those of the present patient. A diagnosis of Madura foot (maduromycosis) was made.

On examination.—Chronic induration both lower legs. Sundry painless ulcers. Sclerosis of skin. Disorganization and shrinkage of tarsus. Peripheral pulses palpable. Knee-jerks present. Minimal wasting of glutei. Sensory impairment affecting impulses from L.4, L.5 and S.1 root areas, bilaterally, thermal and pain sense being more affected than the perception of posture and vibration.

Investigations.—E.S.R. (Westergren): 10 mm. in one hour. Hæmoglobin: 15·4 g. per 100 ml. W.B.C.: 5,000 (normal differential). W.R. and Kahn: negative. Urine: No pus cells. Scanty growth of *B. coli* on culture. Swabbing of ulcer: Hæmolytic streptococcus and *Proteus rettgeri*. Lumbar puncture: C.S.F. clear and colourless. Pressure 110 mm. Manometrics normal. Cells less than 1 per c.mm. Protein 28 mg. per 100 ml. Lange 1111000000. W.R. negative. Serum proteins: Total 8·0, albumin 3·1, globulin 4·9 g. per 100 ml.; A/G ratio 0·6 : 1·0. Alkaline phosphatase: 5 K.-A. units. Thymol turbidity: 8 units. Zinc sulphate: 10 units. Congo red test: 30-minute clearance = 22% (within normal limits). Latex fixation test: Positive. Differential agglutination titre (Rose-Waaler test: 1:1 (32/32) negative.

FIG. 2.—Lateral view of right foot showing gross destruction of phalanges.

X-rays.—Feet: There is gross destruction of the tarsal and metatarsal bones and most of the phalanges of the right foot (Fig. 2). On the left side there is fusion of the tarsal and metatarsal bones with destruction of the majority of the phalanges.

Legs: Gross shaggy periostitis involving the whole of the shafts of the tibiæ and fibulæ.

Lumbar spine: No significant abnormality. Chest within normal limits. Lumbar myelography: A symmetrical and normal appearance was demonstrated from the level of L.1 to the bottom of the spinal theca.

Femoral arteriograms: Normal appearances with the exception of minimal evidence of Mönckeberg's sclerosis in the left superficial femoral artery and diminished vascular supply to the anterior part of the right foot.

Biopsies of skin and muscle were non-contributory to making a definite diagnosis.

Progress and comment.—His skin condition has continued to be well controlled and since coming under our observation in May 1958 no further significant progression of his bony changes has taken place.

This case is thought to be an example of hereditary sensory radicular neuropathy (Denny-Brown, 1951) of the familial form showing typical neurological features. There is no clinical evidence of syringomyelia. It should be stressed that lightning pains and deafness are not features in this particular case.

Biopsy of nerve was not considered a justifiable procedure.

REFERENCE. DENNY-BROWN, D. (1951) *J. Neurol. Psychiat.*, **14**, 237.

(This case will be reported in more detail elsewhere.)

Leukoderma with Loss of Hair. ? Due to Photographic Developer.—K. W. LOVEL, M.R.C.P.

Mr. D. P., aged 50. Photographer.

History.—Had been using photographic solutions for twenty years, with no skin trouble until June 1957, when he noticed discoloration of his palms. This gradually spread up his arms, then to the chest, abdomen, thighs and genitalia. At the same time he noticed loss of hair on the upper parts of the body, but no change in colour of the hair.

Clinical findings.—Leukoderma affecting hands and forearms principally, with loss of axillary hair. No evidence of endocrine disorder.

Investigations.—A slightly raised E.S.R. was the only abnormality found. A patch test with phenidone was negative.

Comment.—The leukoderma appeared nine months after the patient first started using a developer containing phenidone. He was taken off dark-room work in July 1958, since when there has been a gradual improvement. Since January 1959 he has been using another developer, rubber gloves and barrier cream, and the slow improvement continues.

The following cases were also shown:

Occupational Argyria.—Dr. R. J. CAIRNS.

Mercury Sensitivity in a Dental Student.—Dr. BRIAN RUSSELL.

Contact Dermatitis from Cheese Mites.—Dr. J. EVERALL. (With a note on "Food Hygiene in Retail Shops", by Dr. E. W. Gibbs.)

Dermatitis from Multiple Drugs.—Dr. J. EVERALL (for Dr. MITCHELL-HEGGS and Dr. R. D. MOYLE).

Dermatitis from Epoxy Resin.—Dr. M. FEIWEL.

Dermatitis from Chromates.—Dr. M. FEIWEL.

Guttate Morphea.—Dr. STEPHEN GOLD.

Eczema of External Auditory Meatus to Demonstrate an Applicator for Local Therapy.—Mr. A. B. ALEXANDER.

Papulonecrotic Tuberculides.—Dr. E. WILSON JONES.

? Papulonecrotic Tuberculides, Tuberculous Lymphadenopathy.—Dr. Z. CHAMBERLAIN (for Dr. M. FEIWEL).

Neurodermatitis Alba Gigantea.—Dr. H. HABER.

A Symposium on **The Newer Dermatological Hazards of Industry** was introduced by Dr. SIBYL HORNER. Dr. G. HODGSON spoke on **Some New Adhesives and Bonding Materials,** Dr. D. K. HARRIS on **The Skin Effects of Plastics** and Dr. A. J. M. JOHNSTON on **Constitutional and Extrinsic Factors in Cement Dermatitis.**

Meeting
April 16, 1959

Gynæcomastia Persisting after Œstrogen Therapy for Acne.—LOUIS FORMAN, M.D.

Mr. E. G. C., aged 28.

History.—Acne vulgaris of the face, chest and back when aged 14 (1945). Treated with implant of stilbœstrol, two tablets of 100 mg. each. One tablet discharged from wound after two months. The acne improved but relapsed after eighteen months. A second implant of 200 mg. stilbœstrol was made when he was 16, and the acne has remained cleared until the present time. After each implant, the testicles and penis diminished in size, and the breasts enlarged. The genitals have recovered to the normal size and sexual function restored.

Present condition.—The breasts are markedly pendulous and a source of embarrassment to the patient.

Comment.—The effect of large doses of stilbœstrol in the male is well known: (1) Enlargement of the breasts, due to proliferation of the mammary ducts without the formation of terminal acini. The breasts do not lactate—this demands the pituitary hormone of lactation. (2) Diminished activity of pituitary gonadotrophic hormone with regression of the secreting epithelium of the prostate and of the germinal layer of the testis with absence of spermatogenesis. Enlargement, sometimes adenomatous, of the pituitary is seen in experimental animals. It appears to be the general opinion that the changes are reversible when the œstrogen therapy is discontinued. Certainly the genitals recover to a normal size, sexual interest reawakens, erections return, and the sperm count is within normal limits. However, this case illustrates that the enlargement of the breasts, which may be considerable, does persist and demands surgery for cosmetic reasons. Whether these enlarged breasts have a greater potentiality towards malignant changes can only be determined by observation over many years.

In my opinion, œstrogens have no place in the treatment of acne, except perhaps in the cases of acne conglobata, with severe suppuration.

The President: It is important that we should have seen Dr. Forman's patient. We are grateful to him for his exposition of the case. I agree with all Dr. Forman has said in relation to œstrogen therapy for acne in the male.

Dr. H. J. Wallace: I also support Dr. Forman's remarks. Is anything known about the possible impairment of fertility in these patients?

Dr. G. Beck: When the "breasts" are removed it will be interesting to know whether they do in fact contain increased or enlarged true breast tissue or are simply fat deposited at this site.

Dr. M. Garretts: Dr. A. Jarrett has been carrying out research with this form of therapy and he feels there is a place for œstrogens in the treatment of acne. They are of particular value in obtaining rapid control of the acne before using other forms of treatment such as ultra-violet irradiation and local applications. He believes short, reasonably high doses (3 mg. daily for three weeks) can enhance the value of these methods of therapy, and can hasten a good cosmetic result.

Dr. J. G. Holmes: Would it be far less dangerous in this respect if œstrogen were given via the mouth instead of implant?

The President: I feel that small doses of œstrogen are sometimes valuable in the treatment of girls with acne.

Dr. Louis Forman: In my opinion œstrogen therapy of acne in girls may be indicated if there is evidence of œstrogen deficiency provided by a history of scanty or irregular periods. I am guided by the opinion of the gynæcologist in individual cases. The dosage must be small or else troublesome bleeding may result. I agree that there is a considerable amount of fat deposited in the breasts in the male shown.

ADDENDUM.—The breasts when removed contained a large amount of fat, and a few areas of firm white glandular tissue.—L. F.

Kaposi's Sarcoma with a Lung Tumour.—LOUIS FORMAN, M.D.

Mrs. M. L., aged 67.

Past history.—1939: Wassermann reaction positive, no clinical signs of disease. After a course of N.A.B. this reaction was reversed and has remained negative since. Had received injections for many years for pernicious anæmia.

Present disease.—Eight years' history of swelling of the feet and lower legs. When observed three years ago, the skin was diffusely infiltrated and cyanotic, and isolated plaques and nodes were noted up to and above the knees. There was pitting on firm pressure and elephantiasic swelling of the lower legs and feet. The skin of the lower legs has become more normal in colour with increased sclerosis. Other cyanotic nodules have appeared on the knee and leg, in a pattern suggesting a vascular (? venous) localization. Recently there has been complaint of pain left lower chest, referred to the left shoulder. No glandular enlargement.

Investigations.—Biopsy 1957: Capillary proliferation and ectasia, with surround of plasma cells, hæmorrhages, and fibrosis.

Blood proteins, sedimentation rate, blood count and differential are normal, save Hb 74% on one occasion. Direct and indirect Coombs test negative. Test meal—normal acid curve. X-ray chest 1957 reported normal. Repeat X-ray four months ago showed a rounded shadow in the left lower lobe, attached to the diaphragm. When the plate taken in 1957 was re-examined, a faint opacity could be determined, apparently representing an early stage of the tumour now revealed.

Treatment.—1957: Two weeks of penicillin 600,000 units a day with improvement of the colour of the skin and infiltration of the lower legs.

Comment.—The patient was born in Poland and is Jewish. Kaposi's disease, although more frequently seen in Eastern Europe and Northern Italy, has been described in the American Negro and in the Bantu of Africa. There appears to be a geographical distribution of the disease rather than a racial incidence. It is less common in the female (6–10% in reported cases). Although the age incidence is usually between the fifth and seventh decades, Bluefarb (1957) refers to cases which have been described in childhood. There was a period when this patient was said to be anæmic. Anæmia may result from involvement of the gastro-intestinal canal with intestinal hæmorrhage, before there are cutaneous signs. According to Bluefarb, anæmia of the immunohæmolytic type occurs early in Kaposi's disease, comparable to the anæmia seen in other diseases of the reticulo-endothelial system. Cases of primary visceral and glandular involvement emphasize the possible multicentric origin of Kaposi's disease.

REFERENCE

BLUEFARB, S. M. (1957) Kaposi's Sarcoma. Springfield, Ill.

The President: I take it that Dr. Forman regards this as Kaposi's disease, which I feel is infective. Sarcoma sometimes arises in such cases.

Dr. J. E. M. Wigley: I wish Dr. Forman every success with his surgeon. I had a patient whom I looked after for some time at Charing Cross Hospital with an almost identical appearance including the lung shadow. I was never able to persuade the thoracic surgeon to do anything about it. The woman was about 60, and on legs and forearms there were widespread nodules typical of Kaposi's disease. X-ray treatment of these resulted in a considerable amount of temporary improvement.

Professor T. Fitzpatrick: It would be interesting to note the effect of nitrogen mustard on the pulmonary lesion. Kaposi's sarcoma is quite sensitive to intravenous nitrogen mustard in a dosage of 0·1 mg. per kg. body weight given daily for four days.

ADDENDUM.—Mr. R. H. F. Brain performed a thoracotomy and found the pleural surface covered with malignant nodules. The histology of one of the nodules revealed a well-differentiated bronchial carcinoma.—L. F.

Incontinentia Pigmenti.—P. D. SAMMAN, M.D., M.R.C.P.

R. P. P., female, aged 3½ years.

History.—Soon after birth her mother noticed widespread red patches slightly raised but probably without true blister formation. Pigmentation appeared as the patches subsided. She had some eczema on her hands in early infancy.

Present condition.—The child shows the typical bizarre pigmentation of incontinentia pigmenti. In addition she has a mild right-sided hemiplegia,

partial hare lip, and dental abnormalities. Mentality is normal. She speaks Italian, the language of her parents.

Mr. A. G. Taylor gives the following report on the teeth: Of the deciduous dentition five teeth are absent, viz. one upper incisor, two lower incisors and the lower right first and second molars. Furthermore, none of the upper incisors present matches another and the lower incisors and canines are fang-like in shape which is a phenomenon associated with suppression of teeth. Radiological examination disclosed a like condition in the permanent dentition. It is not easy to be completely certain of the teeth present but only two upper and one lower incisor can be seen; only two upper and one lower premolar also. The canines and first molars are all present but no second molars.

Comment.—This case illustrates well several of the other abnormalities frequently reported in association with the pigment changes of incontinentia pigmenti.

Adenoid Basal Cell Epithelioma.—T. HENNEBRY, F.R.C.S., V. B. LEVISON, M.R.C.S., and M. FEIWEL, M.R.C.P.

Mr. A. B., aged 51. Plasterer.

History.—A lump had been present on the back of the neck for twelve years, and had been slowly growing the whole time. It ulcerated three years ago. He never had any pain. The ulcer had bled occasionally. He noticed another lesion on his forehead two months ago.

Clinical findings.—He was admitted to the North Middlesex Hospital in January 1959 with a massive ulcerated tumour on the back of the neck 10 in. in diameter and almost 3 in. thick, with pearly rolled overhanging edges. There was also a second basal cell carcinoma on the left temple. His hæmoglobin was 53% on admission and he was given four bottles of blood.

Biopsy.—Histologically the growth is a somewhat cystic or cribriform type of basal cell carcinoma that presents a honeycomb appearance due to small cystic spaces occurring within the tumour cell masses. The cells that are plump and polyhedral also occur in solid cords as in cylindroma but there is absence of the characteristic hyaline basement membrane of the latter.

Dr. H. Haber considered it to be an adenoid basal cell epithelioma most probably of nævogenic origin.

Treatment.—The basal cell carcinoma on the neck was treated initially with deep X-ray therapy (H.V.L. 2·7 mm. Cu) using two opposing fields 17 × 10 cm., a minimum tumour dose of 5,000 r being given in 40 treatments from 16.1.59 to 20.3.59. There was considerable local improvement, and the growth diminished to about 5 in. in diameter about two months after the radiotherapy was completed. The residual tumour was excised on 28.5.59 by Mr. T. Hennebry, and a skin graft applied from the thigh. The histology of the specimen again showed basal cell carcinoma.

We are indebted to Dr. Ian Gordon for the histology reports.

The President: Had the patient not a lesion on the temple?

Dr. M. Feiwel: Yes, a typical rodent ulcer on the temple which shows the same structure.

Dr. Henry Haber: The histology shows a basal cell epithelioma of the adenoid type. Cylindroma can be excluded as there is no evidence of the presence of hyalin either surrounding the tumour lobes or lying within them.

The following cases were also shown:

Three Cases of Nail Changes Due to Lichen Planus.—Dr. P. D. SAMMAN.

Pityriasis Rubra Pilaris with Tylosis of Palms and Soles and Ainhum-like Constrictions of the Fingers.—Col. P. C. MITCHELL.

Gout.—Dr. O. L. S. SCOTT.

Cerebello-retinal Angiomatosis (Von Hippel-Lindau disease).—Dr. O. L. S. SCOTT.

Porokeratosis of Mibelli.—Dr. A. AITKEN ROSS.

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Section of Odontology

President—W. G. Senior, C.B.E., Ph.D., F.D.S.

Meeting
May 25, 1959

Annual General Meeting at the Royal College of Surgeons, Lincoln's Inn Fields, London

One Hundred Years of the Odontological Museum

By A. E. W. Miles, F.D.S., L.R.C.P., M.R.C.S., and J. W. White, L.D.S. R.C.S.
London

What is now known as the Odontological Museum of the Royal College of Surgeons has to a large extent grown out of the Museum founded by the Odontological Society of London in 1859. The present year is therefore the centenary year of the Odontological Museum. This year is in any case an extremely important one in the history of the Museum; after several years, during which much of it has been in packing cases and the care of it has been associated with much anxiety, the Collection has recently begun to be moved into new quarters which are probably more fitting for it than any it has occupied before. It is indeed a felicitous chance whereby the Museum enters this new phase in its life during its centenary year.

The Odontological Society of London was founded in November 1856 and at first rented accommodation in the rooms of the Medical Society of London at 32A, George Street, Hanover Square. The tenancy of these rooms ceased at the end of 1858 but in the meantime a Committee of the Odontological Society had been very active in planning and bringing into existence the new London School of Dental Surgery and Dental Hospital of London at 32, Soho Square (Fig. 1, p. 855).

On January 8, 1859, at a meeting of the Society held in the new Dental Hospital at the invitation of the Hospital Management Committee, a Committee appointed by the Council of the Society to consider "the best means of rendering the Society more generally acceptable and useful to the profession" reported as follows:

"Great and unquestionable as have been the benefits which the Society has conferred by the Periodical gatherings of its members, its utility might, in the opinion of the Committee, be further increased if it possessed something of a settled home, to which contributions, whether of books, drawings, diagrams, casts, or preparations might be sent, with the certainty of being preserved and arranged, and of being made available for reference or future research. Such an arrangement, however desirable, was not practicable at the former place of meeting, the Medical Society of London having permanent occupancy of all available rooms; but your Committee consider that an opportunity now presents itself for the attainment of this object. Assembled beneath a roof which if it may not strictly be said to be our own, yet belongs in an especial manner to our profession, the Odontological Society would now be justified in incurring a somewhat larger expenditure, to enable it to extend its operations, so far, at least, as to secure permanent occupations of rooms, conveniently situated, suitable for the purposes of a library and museum. Towards the formation of the library a liberal donation of books relating to the Science and Practice of dental surgery has been already received."

The Society's need for a new and larger home expressed in this quotation from the Minutes was quickly met by an arrangement with the Committee of Management of the newly founded Dental Hospital to use its large meeting room and board room for the Society's meetings for the sum of £30 per annum. A few months later in June 1859, for an additional £10 per annum, the Society was granted a tenancy of the front room on the second floor of the hospital "for the purposes of a Museum and Library, such rent to include the opening of the front door by the Hospital Porter". The tenancy of this room commenced on June 24, 1859, and this date may therefore perhaps be accepted as the date of the founding of the Museum.

The first recorded presentation of a specimen to the Society was on April 2, 1859—the skull of a hippopotamus presented by Mr. John Finnie of Alexandria, Egypt, who was elected a corresponding member of the Society shortly after. It seems that this specimen was presented in anticipation of the imminent founding of the Museum. There is some reason, however, to believe that,

even before the events in 1859 that led to the foundation of a Museum, the Society may have possessed some specimens because in the preface to the first catalogue of the Museum issued in 1872 Charles Tomes states that the Museum had been in existence for sixteen years, that is since 1856.

The *Transactions* of the Society record many generous gifts of books long before gifts of specimens; for example, Mr. T. Purland presented in January 1858 a collection of Public Advertisements on Dental Subjects. It is of interest that Purland was not at that time a member of the Odontological Society but was a member of the rival College of Dentists. It would seem that his gift was an act of goodwill towards the "other" Society and is one of the signs in the early records that there were a number of persons who rose above the intense rivalry for which the early relationship between the Odontological Society and the College of Dentists was notable. Purland's gift is now in the Library of the Wellcome Historical Museum.

Arrangements for equipping the Library and Museum were left in the hands of John Tomes and Alfred Canton and it is recorded that the sums of £36 2s. 0d. and £20 8s. 10d. were spent for this purpose.

On February 2, 1859, the Council ordered to be bought a Book of Benefactors in which was to be recorded the donation of books, money and other property. An entry in the Minutes of the general meeting of January 9, 1860, reads, "The entire list of presentations to the Library and Museum during the past year was read from the Book of Benefactors". This custom of reading formally to the Council of the Society a list of gifts appears to have been discontinued after 1872 as there are no further records of such readings in the Minutes. It would seem likely to have been replaced by the custom, which persists to this day, whereby the Honorary Curator presents a Report on the Museum to the Annual General Meeting of the Society. The original Book of Benefactors is unfortunately no longer extant.

The first Curator of the Museum was Edwin Sercombe who was appointed on April 11, 1860. He held office only until the following November when he resigned because he was no longer resident in London. He was succeeded by Mr. W. F. Forsyth who held the appointment until 1864.

An important event in the early history of the Museum was the amalgamation of the College of Dentists with the Odontological Society in 1863. This event was of importance because the College of Dentists brought with it the Library and Museum which it had possessed from the early days of its foundation in 1856. An entry in the Minute book of 1863 of the College of Dentists reads, "Resolved that Mr. Hulme be requested to arrange for the removal of the Museum and Library to Soho Square before the first Monday in June". Mr. R. T. Hulme was the Librarian and Curator of the College's Museum.

The College of Dentists might have claimed to be two or three years in advance of the Odontological Society in respect of a Museum, because the College appointed its first Librarian and Curator, C. J. Fox, in 1857. Fox was succeeded by T. Purland in 1858 and he in turn was succeeded in 1862 by R. T. Hulme who, as previously mentioned, was Curator at the time of the removal of the Museum of the College of Dentists to Soho Square.

The exact size and scope of this acquisition by the Museum of the Odontological Society is not known for certain but there is reason to believe that it was quite substantial and may well have been comparable with that of the Odontological Society at that time. Gifts of specimens are frequently recorded in the reports of meetings of the College of Dentists published in the *British Journal of Dental Science* (1857–63); for example at least 53 specimens were presented in 1857 and about 66 in 1862.

Unfortunately no distinguishing marks were attached to the College of Dentists' specimens, and at the present time it is only possible to identify a very few specimens as probably being original College of Dentists' specimens.

In 1864 Forsyth was succeeded as Curator of the Odontological Society's Museum by Nathaniel Stevenson.

In the original agreement with the hospital authorities no provision seems to have been made for keeping the Library and Museum clean. This appears to have been the cause of a series of troubles extending for several years in the early history of the Museum. For example, trouble arose in 1865 over the dirty condition of the Museum in the course of which Stevenson, the Curator, tendered his resignation on the ground of incivilities that had been offered him by a Mr. Glover who was apparently the hall porter at the hospital. At the request of the President, Mr. Stevenson attended a Council meeting and with-

drew his resignation on being informed that Mr. Glover was not a servant of the Society and that the Council therefore had no jurisdiction over him. Stevenson stressed to the Council the need to appoint someone whose duty would be to cleanse the Museum, dust the glass cases and maintain it in a good state. It was left for the President to make some suitable arrangement but it may be suspected that he found no solution because Stevenson resigned the office of Curator a few months later. He was succeeded in 1865 by R. T. Hulme who had been the Curator of the College of Dentists. It is interesting to note that at this time a proposal that the Curator should be

who was 24 years of age and had qualified L.D.S., M.R.C.S., only the year before. The first catalogue of the Collection was issued in 1872 after two years of extensive work by Charles Tomes, aided by his friend Mr. J. Scully, to whom Tomes acknowledged his indebtedness "for his co-operation in the arduous task of arranging a chaotic assemblage of unnamed specimens". Mr. Scully was a member of the Society, having been elected in 1870.

There are slightly more than one thousand entries in the 1872 catalogue but the actual number of specimens was much greater because

FIG. 1.—A drawing by Hanslip Fletcher showing 32, Soho Square (the building in the corner with the elaborate windows and balcony), just prior to its demolition in 1937. Reproduced by kindness of J. A. Donaldson, Curator, British Dental Association.

ex officio a member of the Council was not adopted on the grounds that there were already a sufficient number of *ex-officio* members. At this distance of time the Council's attitude is hard to understand because the Librarian had been a member of the Council since 1861.

In 1868 Hulme drew attention to a need for more space for the Museum, which still shared a room with the Library. It was agreed to provide more room for the display of specimens by transferring two large bookcases to the "large operating room" of the hospital. In 1870 Hulme was succeeded as Curator by Charles S. Tomes

some entries refer to groups of specimens. Three special collections had been on loan from Samuel Cartwright, Junior, W. A. N. Cattlin and John Tomes for some years and these in subsequent years became permanent parts of the collection, the Cartwright Collection for instance being formally presented by S. Cartwright, Junior, in 1885.

Many early specimens, including some from the Cartwright, Cattlin and Tomes collections, can be identified among our present specimens and no doubt continued diligent search would reveal others.

In 1874, the London School of Dental Surgery, having outgrown the accommodation in Soho Square, acquired a building in Leicester Square and converted it into a new Dental School and Hospital (Henry, 1955). The Odontological Society with its Library and Museum was transferred to the new dental school and part of the collection was displayed on the first floor and in the gallery surrounding the lecture theatre. The Odontological Society's Museum was thus an amenity enjoyed by the students of the hospital and indeed was used by students of other hospitals; for example in 1877 a request was granted for "Mr. Gaddes, the teacher of dental anatomy at the National Dental College, Great Portland Street, to pay periodical visits to the Museum of the Society with his pupils".

It is clear from careful reading of the Minutes of the Society that the fortunes of the Museum underwent fluctuations. In 1879 there appear to have been difficulties and the Curator, Charles S. Tomes, supported by Alfred Coleman, appealed to the Society for paid assistance in preserving and cataloguing the specimens. A committee set up to consider the matter inspected the Museum and arranged for someone to dust and clean the specimens. J. B. Major and W. Weiss were also appointed to describe and arrange specimens and were paid an honorarium of 10 guineas each. Weiss was a member of the Society, having earlier been a member of the College of Dentists. J. B. Major has not been traced in the membership lists.

In 1880 S. J. Hutchinson was appointed Curator and during the following few years a good deal of reconstruction and expansion took place. The sum of £75 was spent on new showcases. In 1874 John Bland-Sutton presented many of his specimens of comparative dental pathology and also sold to the Society, for the nominal sum of £15, a large showcase to accommodate them.

Hutchinson produced a new edition of the catalogue in 1882 in which the number of entries had risen to over 1,500. Unfortunately the names of donors of specimens, which provide the principal means of tracing specimens of that early period, were not in every case transferred to the new catalogue.

In 1885 Storer Bennett became Honorary Curator. During his curatorship a paid Museum assistant was employed sporadically, at one time by the Society and at other times out of the Curator's own purse sometimes at the rate of £1 per week and sometimes for one shilling or 1s. 6d. per hour. No stable and satisfactory solution was found, however, to the problem of the day-to-day cleaning and care of the Museum; for example, at a Council meeting in 1890 the Curator had to report that he had been obliged to discharge the Museum Assistant, having on two occasions found him intoxicated.

The loan of specimens is always a source of much anxiety to those in charge of a museum, and it was during Storer Bennett's period of office that the risks so run were brought to light. Permission was granted for specimens to be sent for exhibition at a meeting of another Society. A series of preparations illustrating points of interest in comparative dental pathology was accordingly carefully packed by the Curator in tissue paper, enclosed in wooden boxes, and put into packing cases; it arrived uninjured at its destination. To quote Storer Bennett's words, as recorded in the Minute book (November 5, 1888), the specimens "were returned to our museum very considerably damaged from the utter disregard to their character that has been shown by the person who packed them; in many cases they were wedged into the boxes by brown paper or shavings. The result is that bones have been broken, teeth knocked out and lost, and in some instances the specimens were not returned at all, or only in part". Fortunately this source of possible damage to specimens has since been removed by the rule now in force forbidding their loan for exhibition at meetings other than those connected with the Odontological Section of the Royal Society of Medicine.

In 1900 Storer Bennett died suddenly and Sir Frank Colyer was appointed. This occurred at a time when negotiations were under way to transfer the Museum at least temporarily from the London School of Dental Surgery to the Royal College of Surgeons. These negotiations stemmed a few years earlier (1891) from the need of the Dental School and Hospital for the space occupied by the Odontological Society, and finally from the transference of the Dental School and Hospital to its present site. The collection was therefore, in 1900, packed up and transferred to the Royal College of Surgeons, but less than a year later the Odontological Society had found new premises. In October 1900 it entered into occupation of part of the premises of the Royal Medical and Chirurgical Society of London at 20, Hanover Square and the Museum was allotted a large L-shaped room on the third floor.

Fig. 2 shows the interior of the Museum in Hanover Square and is unfortunately the only

FIG. 2.—A view of the Odontological Museum in 20, Hanover Square.

photograph in existence of the Collection in any of its various resting places.

In 1907 the long contemplated formation of the Royal Society of Medicine took place, and the Odontological Society became its Odontological Section. The Royal Society of Medicine at first occupied 20, Hanover Square so that the Museum remained undisturbed. In September 1909, however, in anticipation of a projected temporary move of the Society to 15, Cavendish Square until the completion of the new building at 1, Wimpole Street, the custody of the Odontological Museum was, by deed of transfer, handed over to the care of the Royal College of Surgeons. The collection, which at that time consisted of about 2,900 items (Colyer, 1943), was housed in a large semi-basement room which, as many will remember, was reached by a staircase behind Hunter's statue at the far end of the old Room II of the Royal College of Surgeons Museum. The agreement between the Royal Society of Medicine and the Royal College of Surgeons at that time provided that in the event of the Society desiring the return of the Collection "only those specimens forming the Collection at the time of the transfer should be returned and not those added since the transfer". The Museum became integrated with the Museums of the College under the Conservatorship of Sir Arthur Keith who permitted the transfer to the Odontological Museum of certain Hunterian specimens, including those used by Hunter to illustrate his "Natural History of the Teeth". The full and formal title of the Old Odontological Society's museum became, and still is, the Odontological Series of the Royal College of Surgeons Museum.

On the outbreak of war in 1939, steps were taken to preserve and protect the Collection and, although in 1941 the College and its Museums were very severely damaged, by good fortune the Odontological Series escaped more or less unscathed.

In 1943 those specimens in the Collection which had formed the Odontological Museum before its transfer to the Royal College were offered by the Council of the Royal Society of Medicine as a goodwill gesture towards the reconstitution of the grievously damaged Museums of the Royal College of Surgeons. The College gratefully accepted them and thereby the relationship of the Odontological Section of the Royal Society of Medicine and what had been its Museum underwent a change. The Odontological Section still retains its connexion, however, by these Annual General Meetings and by retaining the right to be consulted regarding the appointment of the Honorary Curator.

In 1950, in connexion with the rebuilding of the College, the Odontological Series had to be packed up and moved from the rooms it had occupied for forty-one years. Since then much of the Collection has had to be stored, but for several years a substantial portion has been displayed in the Wellcome Museum of Pathology.

FIG. 3.—The recently opened Odontological Museum at the Royal College of Surgeons.

At the present time, however, the Collection is in process of being moved to its very fine new quarters on the first floor of the new building, very appropriately alongside the Department of Dental Science. The new accommodation consists of a large, imposing and well-lighted room (Fig. 3), adjoining which is a preparation or Curator's room.

It is a remarkable fact that for more than one-half of the hundred years the museum has been in existence, that is from 1900 until his death in 1954, it was in charge of one Curator, namely Sir Frank Colyer. Through his indefatigable efforts the size of the Collection more than doubled, towards the end of his lifetime being significantly enlarged by the unostentatious gift of his own personal collection of skulls.

Sir Frank's principal purpose during his Curatorship was to make the museum into much more than a shop window of specimens. His purpose was to gather a collection of material which by careful study could be used for the advancement of knowledge. Although the direct value in biological research of museum collections of material may have passed its zenith—the emphasis now is quite properly on the experimental approach and upon new tools provided by histology and chemistry—no one would deny that this great collection, which was built up in the way described here and which probably is unequalled anywhere in the world, must be carefully preserved for all time.

Acknowledgments.—We have drawn freely upon manuscript notes left by the late Sir Frank Colyer.

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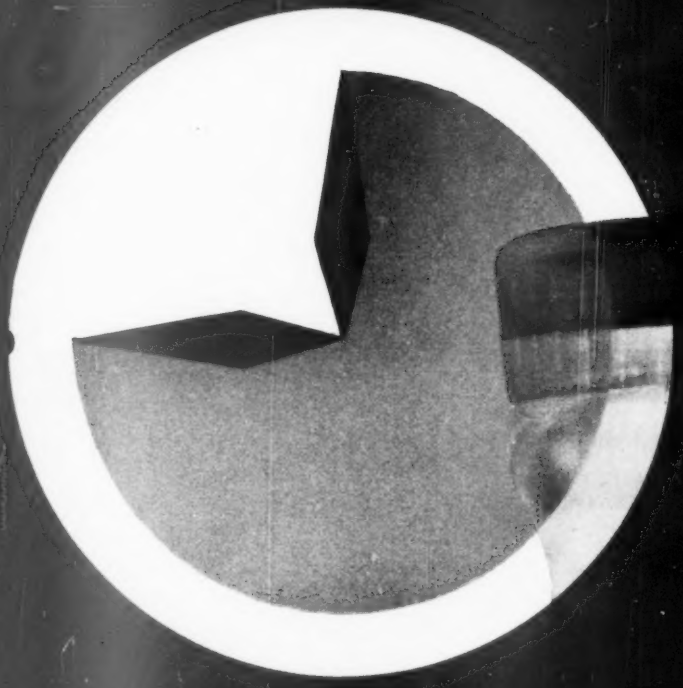

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Section of Orthopædics

President—J. S. BATCHELOR, F.R.C.S.

Meeting
April 4, 1959

MEETING AT BIDDULPH GRANGE ORTHOPÆDIC HOSPITAL, STOKE-ON-TRENT

CASES

IN the morning the Section examined a most extensive and rewarding demonstration of cases by Sir Harry Platt, Mr. Denys Wainwright, Mr. C. S. Walker, Mr. A. Kennard Mitting, and their staff. Among the cases shown were the following:

Twenty Cases of Osteoarthritis of the Hip-joint.—Mr. DENYS WAINWRIGHT.

These were treated by the McMurray displacement osteotomy. Several of the patients had been under observation for ten to fifteen years, and in these a plaster spica was used for post-operative immobilization. In the more recent cases internal fixation had been secured by the use of a straight blade plate.

Cases of Slipped Upper Femoral Epiphysis.—Sir HARRY PLATT and Mr. DENYS WAINWRIGHT.

These cases illustrated the use of internal fixation either by Smith-Petersen pin or Moore's pins in those cases with a minimal slip. Three cases of subtrochanteric osteotomy performed for irreducible slipped epiphysis were also shown.

Septic Arthritis of the Hip-joint.—Mr. DENYS WAINWRIGHT.

The results of reconstructive procedures following destruction of the femoral head and neck in infancy. These included (*a*) examples of arthrodesis of the hip-joint associated with femoral lengthening and (*b*) extra-articular shelf operations to increase stability and prevent further upward displacement of the femoral shaft.

Congenital Dislocation of the Hip-joint.—Sir HARRY PLATT and Mr. DENYS WAINWRIGHT.

A number of cases were illustrated to demonstrate the importance of early diagnosis. Other cases included examples of extreme anteversion, the use of the extra-articular shelf operation and the Schanz osteotomy for old unreduced congenital dislocation of the hip.

Mid-cervical Fractures of the Femur.—Mr. DENYS WAINWRIGHT.

Treated by gradual reduction and fixation by low-angle Garden-type lag screws.

Congenital Pseudarthrosis of the Tibia and Fibula.—Mr. DENYS WAINWRIGHT.

Several cases were shown, including one case in which union had eventually been obtained by intramedullary fixation and osteoperiosteal grafts after two failures by by-pass grafts.

Osteoid Osteoma.—Mr. DENYS WAINWRIGHT.

Examples of osteoid osteoma included two cases of giant osteoid osteomas—fibula and olecranon—and other cases involving the tibia, astragalus and neck of femur.

Fractures of the Shaft of the Femur and Humerus.—Mr. C. S. WALKER.

Cases illustrating the use of the Küntscher nail for certain difficult fractures of the femur and, with onlay bone grafts, for un-united fractures of the humerus.

Scalenus Anticus Syndrome.—Mr. A. KENNARD MITTING.

Three cases of scalenus anticus syndrome treated by division of the scalenus anticus muscle from its insertion. The muscle was found to be contracted into a tight band in all cases. Complete relief of symptoms resulted. These three cases are typical of a large series carried out.

SYMPOSIUM ON INDICATIONS FOR INTERNAL FIXATION OF SHAFT FRACTURES OF THE LONG BONES [*Abridged*]

Mr. Norman Roberts (Liverpool):

Indications for the Use of Metal

Metal can be used in the treatment of fractures of the long bones for three distinct reasons: (1) To secure a better reduction of displacement than can be achieved by conservative treatment. (2) To assist union. Metal may be a cause of delayed or non-union, but it can assist union when combined with bone-grafting or by achieving primary reduction of a widely displaced fracture. (3) To provide rigid internal fixation so as to reduce or abolish the necessity for external fixation.

The disadvantages of the use of metal are the same as they have always been: (1) Mechanical failure: this may result from the personal failure of the surgeon to apply a workable method, or from the adoption of an unsound method. It may also occur if the surgeon attempts to use metal for the fixation of fractures where the mechanical difficulties are too great to be over-

come. (2) Delayed or non-union. There is no doubt that in certain circumstances metal hinders bony union. (3) Sepsis: I include under this broad heading any "trouble" arising from the use of metal whether from infection, early or late; corrosion; mechanical pressure and irritation; or failure of wound healing.

The surgeon's task is to weigh these advantages and disadvantages as they apply *in each individual case* (not in an "unselected series"). He will, as his experience grows, come to some general conclusions about the indications for the use of metal. My own general conclusions, as they apply to each of the major long bones, are as follows:

Tibia.—There is no need for the use of metal to secure reduction in the large majority of cases. Good position can be secured by conservative treatment. The probable incidence of "trouble" in this bone is around 10%, and that is much too high a price to pay for improved reduction.

There seems to be no indication for the use of metal in order to assist union.

It has been claimed that metal should be used in the tibia for the purpose of rigid internal fixation with a policy of early ambulation without external protection. In theory this is the ideal treatment and there is no room for complacency about the harmful effects of long immobilization when tibial fractures are treated conservatively. If a method could be found and proved, either by metal or by any other means, whereby reduction, union, and freedom from immobilization can be achieved safely it will soon be universally adopted. Publication of results in carefully selected (not unselected) cases might well define the usefulness of this method and its safe limits. Until this has been done I shall continue to avoid the use of metal in the tibia.

Humerus.—I do not use metal in the primary treatment of fractures of the shaft of the humerus. Serious delay in union is rare in the ordinary civilian injuries. If it occurs grafting should be early, say at three to four months, and an intramedullary nail with cancellous bone grafting is probably better than the use of cortical bone without metal.

Femur.—As in the tibia, reduction of displacement is only occasionally undertaken with the use of metal, e.g. where severe muscle interposition is present and in certain subtrochanteric fractures. In the latter the metal may be in the form of a Smith-Petersen pin and long plate rather than an intramedullary nail, and this is my personal preference. Metal is also indicated in the form of an intramedullary nail in the elderly, in multiple injuries, and in combination with cancellous bone grafting for the treatment of non-union.

Metal can also be used in the femur for the purpose of rigid internal fixation so as to dispense with external fixation. As in other long bone fractures it is a question of weighing up the possible complications and disadvantages before making a decision in any particular case. I still use conservative treatment in a Thomas splint in the majority of uncomplicated shaft fractures.

Forearm.—Here the argument in favour of using metal is much stronger, partly because accurate reduction is necessary to restore rotation movements, and partly because metal is tolerated so much better in the forearm with a high resistance to potential infection as compared with the prospects in the subcutaneous and poorly nourished tibia.

Fractures of radius alone.—In a series of cases recently reviewed at the Liverpool Royal Infirmary there were 20 cases of the Galeazzi fracture treated by plating. In 18 there was an excellent result without complication. One was poor on account of mechanical failure from bad surgery. One was complicated by sepsis which healed after removal of the metal, but in the meantime mechanical failure had resulted and the functional result was poor. There were no cases of non-union.

Fractures of radius and ulna.—The general practice has been to reduce and plate the radius, and to rely on reduction alone for the ulna, without plating. Some of the cases reviewed would have had more perfect reductions if the ulna had been plated. There were 25 cases. Sepsis occurred in 2; one in plating of the ulna and the other where Kirschner wires were used for both bones and were left protruding through the skin. There was no case of infection from plating of the radius. There were no cases of non-union in the radius. There were two un-united fractures of the ulna, one symptomless and the other later successfully grafted.

Monteggia fractures.—There were 10 cases. None was complicated by sepsis. There were 2 cases of non-union, both successfully grafted.

Conclusions.—The use of metal is indicated: (1) In the tibia only on rare occasions. (2) In the femur for the management of special problems, such as multiple injuries, and also in subtrochanteric fractures and as part of the surgical treatment for non-union. (3) In the humerus as part of the treatment for non-union. (4) In the forearm, as the treatment of choice in most cases to secure accurate reduction.

Mr. F. W. Holdsworth (Sheffield):

I think that during the past half-century, orthopædic, and indeed all, surgeons have been far too concerned with techniques rather than indications. There is a tendency to assess the ability of a surgeon by the brilliance of his operative technique, rather than by the soundness

of his judgment. We tend to forget that operations expose our patients to a risk, and that the results of failure of an operation may be and often are disastrous.

It is customary nowadays to assess the success of any surgical procedure statistically—to show, for example, that only 3–4% of femoral fractures treated by intramedullary nail become infected. Such figures give a totally misleading impression, for the results of any failure may be so crippling and appalling that no thinking surgeon would lightly subject a patient to such a risk.

Nevertheless, the development of better techniques of internal fixation and of better materials makes this method useful in the treatment of long bone fractures in the right patient.

The object of treatment of a long bone fracture is to restore the limb to full functional activity. To achieve this object the broken bone fragments must be placed in apposition and in reasonable alignment and immobilized until union is sound. This can be achieved either by manipulation and external splinting or by operation, with or without internal fixation. In general, much more accurate alignment can be obtained by operation than by manipulation. Experience in the treatment of fractures shows that at least for most long bones accurate re-alignment of the fragments is not necessary for the restoration of full function.

In most of these fractures satisfactory alignment can be obtained by simple manipulation, or by simple manipulation and traction. When satisfactory position has been obtained then the fragments must be immobilized in this position until union is sound. Generally external splinting if properly applied provides a simple and safe method of immobilization, preventing the recurrence of angulation or rotation, whilst overlap can be prevented by continuous traction. Continuous traction has been condemned as a potent cause of non-union, but, in my experience, if properly applied so as not to distract, is less frequently associated with non-union than internal fixation.

The indications for open reduction and for internal fixation in these fractures are: (1) Inability to obtain by manipulation sufficiently good alignment to be consistent with the restoration of good function. This may be due to the interposition of soft tissues between the fragments or the necessity of obtaining completely accurate reduction as in fractures of the forearm, for any displacement in these fractures will result in loss of some degree of pronation and supination. (2) Inability to maintain satisfactory position by external splinting with or without continuous traction, a difficulty again most obvious in fractures of the radius and ulna, where in my experience no form of external splint will maintain position. In the other long bone fractures I believe that though open reduction may be necessary to obtain satisfactory position internal fixation is not necessary to maintain that position, though I confess that having exposed my patient to the dangers of open reduction I then often use internal fixation to maintain position. (3) To allow earlier mobilization of joints, especially the knee-joint in femoral shaft fractures. Unless the internal fixation is by intramedullary nail, joint immobilization is necessary for as long as or even longer than with conservative measures, and in my experience, even with the intramedullary nail, an equal range of joint movement is recovered after conservative treatment, though a much longer time is necessary.

It is as well to remember that internal fixation never assists union of a fracture—the most that can be said is that it may not interfere with union and that it always exposes the patient to an additional risk.

Mr. John Charnley (Manchester):

I want to confine my remarks to biological considerations of what is actually happening between the broken ends of bones during the union of a fracture. This has a profound influence on our decision whether or not to treat a patient by internal fixation. There are many who believe that open reduction and internal fixation impede the normal process of fracture repair, though opinions differ as to how important the delaying action of open reduction may be. The decision to use internal fixation is therefore based on reasons such as economic expediency or clinical experience rather than on the logic of biology. The attitude of mind to be encouraged is not to regard internal fixation as the ideal to strive for whenever possible, but as a method which clinical experience has shown to cause less harm *in certain special cases* than conservative measures. Unless we employ a bone graft there is no method of initial treatment of a fracture of the shaft of a long bone which will enhance or accelerate the power of union.

We have to face a certain fatalistic attitude to fracture union in that the natural potential for union has probably been decided by the magnitude of the displacement of the fragments at the time of the injury. Gross displacement tears soft parts, and it is in the soft parts, and especially at the attachments of interosseous ligaments or intermuscular septa, that callus seems to spread from bone to bone. Callus cannot jump a gap if there is no pathway of soft parts to conduct it across. If a callus pathway is not present, the callus will heap up at the bone end without flowing across the gap. The greatest advance in the treatment of fractures of the long bones lies not so much in improvements of methods of internal

fixation as in the use of small bone grafts of autogenous iliac bone, according to the Phemister principle, inserted subperiosteally about three months after the injury, or as soon as delayed union is first suspected. In this way steps are taken before the fracture passes into the more difficult state of pseudarthrosis.

Mr. C. S. Walker (Stoke-on-Trent):

Review of 49 cases of Fractured Femur Treated by Intramedullary Küntscher Nailing

Since 1951, 49 cases of fractures of the shaft of the femur have been treated by open reduction and fixation with an intramedullary Küntscher nail. None of the cases was nailed as an emergency. All had preliminary skeletal traction by means of a Kirschner wire through the head of the tibia and the nailing was performed at the most convenient time, compound fractures being delayed until the original wound had healed. The minimum time was two days and the maximum seven weeks, apart from two cases treated for non-union where it was three months.

All the cases were treated by open operation using an antero-lateral incision, retraction of the anterior border of vastus lateralis and splitting of vastus intermedius only. A minimum amount of muscle stripping was performed, only sufficient to enable the fractured ends to be grasped by strong bone-holding forceps. The nail was inserted in a retrograde manner, hammered out through the trochanter and its proximal end exposed by a small stab incision. Use of reamers in the later cases has made the operation easier, ensured a better fitting nail and caused less damage to the trochanter.

Indications.—The ideal indications appeared to be those cases in the upper third of the shaft where the medullary cavity was narrow and of fairly uniform diameter, those that were not comminuted and those that were not too oblique. Such cases gave perfect immobilization and no external fixation of any kind was required. Unfortunately, only a small proportion of cases fall into this ideal category; in this series only 14 cases. Therefore, the method was tried for less ideal indications, where nailing alone did not give such perfect immobilization. 27 of the cases had some form of external splintage, usually a Thomas splint followed by a caliper, sometimes plaster; 7 of these, however, had other fractures in the same limb. 6 of the cases were in the lower half where the medullary cavity was wide. With temporary external splintage, and the maximum length of nail, satisfactory union could be obtained. 3 of the cases were double fractures.

Multiple injuries.—11 cases had other fractures of the same limb. (*a*) *Fractured patella:* 5 cases had fractures of the patella, 3 with marked separation, 2 without displacement. The 3 with displacement had the patellæ excised at the same operation as the nailing. The other 2 had temporary splinting. One of the cases is recent; the other 4 regained full, or almost full, movement of the knee. (*b*) *Fractured tibia and fibula:* 3 of the cases had fractures of the lower leg in the same limb. (*c*) *Pott's fracture:* 3 of the cases had fractures around the ankle treated by plaster immobilization after nailing of the femur.

Age.—Ages varied from 15 to 80 years. (1) *Elderly:* 5 of the patients were over 69. The method is particularly valuable for older patients who do not tolerate long periods of immobilization. It is an easier operation in old people because they do not have the well-developed muscles of the young adult and there is a wide medullary cavity which will take the largest calibre nail. (2) *Teenage:* 6 of the patients were in their teens, 2 aged 15 only. Cases as young as this are probably not suitable unless there is some special indication.

Compound fractures.—7 of the cases were compound, varying from small puncture wounds to large wounds with the fracture-ends protruding. All had delayed nailing after primary excision and suture of the wounds and a period of skeletal traction. All 7 united satisfactorily, although some were slow in consolidating. Nothing is gained by emergency nailing and a possible disaster may result.

2 cases were nailed for delayed union.

Complications.—Mortality: One patient, aged 80, collapsed and died the morning after operation. *Sepsis:* One patient, nailed for non-union, developed an abscess one month after operation followed by a persistent sinus. *Delay in union:* 3 cases angulated or refractured because the nail was removed too early. All 3 united satisfactorily with plaster or caliper. One other case failed to consolidate and the nail fractured eleven months after operation. The proximal half of the nail was removed and an onlay bone graft produced consolidation. Apart from the case of sepsis, all other cases united satisfactorily. *Fat embolism:* One case became comatose ten days after operation but recovered. He had fractures of both humeri in addition to the fractured femur. *Shortening:* One case united with 1½ in. (4 cm.) of shortening because of obliquity and a large loose fragment. The other cases had inappreciable shortening. *Knee movement:* 40 cases could be followed up for a sufficient length of time. 29 regained full movement of the knee, 9 had 90 to 130 degrees of movement and 2 only had less than 90 degrees, one 70 degrees, the other 80 degrees.

Conclusions.—(1) That intramedullary nailing is the method of choice in all suitable cases of

fracture of the shaft of femur in adults. (2) That it is especially indicated in: (*a*) Cases of multiple injuries in the same limb. (*b*) Elderly patients. (3) That nailing in compound fractures should be delayed until the original wound has healed. (4) That removal of the nail should be delayed until it is certain that consolidation is complete. (5) That nailing is of value in cases of non-union. Further study should indicate whether or not bone grafting in addition is necessary.

Mr. J. E. M. Smith (Stoke-on-Trent):

The Timing of Internal Fixation

In a recent review of fractures of the forearm treated by internal fixation it was noticed that there were marked variations in the time taken to obtain union; some showed advanced union within ten weeks whilst others were still not united ten months or more after injury. It was later found that a number of fractures showing rapid union had been operated upon some days after injury and further investigation showed that all seventeen non-unions encountered in this series had occurred in patients operated upon in the first six days. In a group of 52 fractures operated upon after the sixth day, all cases proceeded to union, 50 of them within six months of injury. Both early and delayed operations had been carried out by the same team of surgeons, and the two groups were found to be comparable from every important aspect; the evidence has been fully documented elsewhere (Smith, 1959). Delayed internal fixation in the forearm carries a greater risk of cross union, but this risk is probably small compared to that of non-union from early internal fixation.

I have recently carried out a similar investigation on fractures of the shaft of the femur treated by internal fixation and the results have shown a remarkable similarity to those obtained in the forearm; these are shown in Table I.

TABLE I.—FRACTURES OF SHAFT OF FEMUR

Early operation	*Delayed operation*
(1st to 6th days)	(Mainly 2nd and 3rd weeks)
16 fractures	30 fractures
3 re-fractures following removal of nail	No re-fractures
3 non-unions which required bone grafts	No non-unions.

It should be mentioned that 5 of the 6 cases of re-fracture or non-union shown in Table I had been operated upon by consultant surgeons with considerable experience. It should also be stated that the series of fractured femurs treated by early fixation was a very favourable one with a young average age and only two compound injuries. In the group treated by delayed fixation, the average age was considerably higher and there were seven compound injuries, some very severe. The total figures obtained to date are shown in Table II.

TABLE II.—RESULTS OF INTERNAL FIXATION FOR FRACTURES OF SHAFTS OF RADIUS, ULNA AND FEMUR

Early operation	*Delayed operation*
(1st to 6th days)	(Mainly 2nd and 3rd weeks)
94 fractures	82 fractures
20 non-unions	No non-unions
3 re-fractures	No re-fractures

I have no doubt that the "delayed" series of fractures in both forearm and femur have been exceptionally favourable ones, and that the complete absence of non-union in both groups is certainly fortuitous. I am convinced, however, that the advantages of delayed fixation in the prevention of non-union are so great as to merit consideration in the majority of shaft fractures of the long bones in which internal fixation is indicated.

Acknowledgment: My thanks are due to Mr. C. S. Walker for permission to review a number of his patients.

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Dr. L. S. Michaelis (Stoke Mandeville):

Indications in Paraplegic Patients

In paraplegics who fracture a long bone at the time of their spinal injury, fractures of the humerus and forearm should be plated as soon as the general condition permits. The reasons are: (1) That plaster or splinting is ineffective or dangerous in a bed-patient who has to be turned two-hourly. (2) That good alignment and full joint range are doubly important in patients whose upper limbs may have to become weight-bearing if paralysis of the lower limbs persists and the patient has to walk on crutches.

In the lower limb primary internal fixation has not been needed. Alignment and union could be achieved with well-padded splints and very light skin traction.

Skeletal traction should be avoided because of the dangers of overpulling and pressure-sore development at the traction site.

In 2 cases of non-union after four months, internal fixation of femur and tibia respectively became necessary. Non-union was due to overpulling by skeletal traction used outside in the first case, to infection of a compound fracture in the second. In the femur a long lateral plate was combined with a short anterior sliding graft. Union occurred in four months.

The Symposium was summarized and brought to a conclusion by **Sir Harry Platt** (Manchester).

Some Problems in the Treatment of Disorders of the Hip-joint in Various Age Groups

By DENYS WAINWRIGHT, M.Ch.Orth., F.R.C.S.

Suppurative arthritis of infancy.—In 1874 Thomas Smith described a series of cases of suppurative arthritis of infancy which differed in many respects from septic infection of joints in older children or adults. The article was illustrated by a series of wood-cut engravings demonstrating the underlying pathology—a hæmatogenous osteitis of the juxta-articular bone.

We have recently reviewed the cases of septic arthritis of the hip-joint which have been under treatment at the Orthopædic Hospital, Stoke-on-Trent, and Biddulph Grange Orthopædic Hospital during the last fifteen years. The total number of cases was 64. In 16 cases the onset of the disease occurred within the first six months of life and, of these, 11 cases were under 6 weeks old. The predominant organism was the *Staphylococcus aureus*, and in the last 3 cases the organism was penicillin-resistant.

Recent work by Trueta (1957) and others has clearly demonstrated the precarious nature of the blood supply of the femoral head in infants. Any septic infection of the neck of the femur resulting in abscess formation with distension of the joint may rapidly deprive the femoral head of virtually the whole of its blood supply and these destructive changes are likely to occur even more rapidly if a pathological dislocation is allowed to occur, accompanied by kinking and traction of the circumflex vessels running in the joint capsule. If we are to avoid such disastrous results, early diagnosis and treatment are essential.

The early signs of joint inflammation in an infant are not easy to detect—a little peri-articular swelling, possibly slight discoloration of the skin, excessive irritability on handling, pseudo-paralysis and signs of a general infection, although the latter are often slight. Any tenderness or relative immobility of a limb, with or without swelling of the overlying soft tissues, is more likely to be due to infection than any other cause, and the primary site of the infection is much more likely to be in bone than in the subcutaneous tissues.

Treatment.—In view of the frequency of penicillin-resistant staphylococcal infections the infant should be treated with a wide-range antibiotic, at any rate until the nature of the infection and the sensitivity have been established by aspiration of the hip. In addition to aspiration or arthrotomy when necessary, the joint itself should be immobilized in abduction and, if necessary, traction applied, and this position maintained during the period of active inflammation and for some weeks afterwards. Every effort to prevent a dislocation of the joint occurring is well worth while, as during the subsequent weeks and months complete or partial restoration of the upper end of the femur may occur, and the preservation of some type of femoral head will make reconstructive procedures very much easier in the future.

In those cases in which more or less complete destruction has occurred with dislocation and instability, an attempt should be made at some time to stabilize the joint. We have, on the whole, been disappointed with the results of hip reconstructive procedures in the young child. Even though stability may appear to have been obtained, as growth proceeds this is usually lost. Gross upward displacement of the femoral shaft can to some extent be prevented by wearing a weight-relieving caliper until at an appropriate age some type of arthrodesis is performed.

In a few patients we have endeavoured to obtain stability of the hip-joint and prevent further upward riding of the femoral head by performing an extra-articular shelf operation, turning down the outer table of the ilium over the remains of the upper end of the femur and great trochanter (Fig. 1). Some of these cases have

FIG. 1.—Extra-articular shelf used to stabilize pathological dislocation of the hip following septic arthritis.

FIG. 2.—Subtrochanteric displacement osteotomy for irreducible displacement of the upper femoral epiphysis.

been observed for several years and have a pleasing degree of stability and freedom from pain. If, however, we can recognize acute infections of the hip-joint occurring in infants at an early stage, adequate treatment by the administration of the appropriate antibiotics and immobilization of the joint in a position of abduction will render such extensive surgical procedures unnecessary.

Slipped upper femoral epiphysis.—There is fairly general agreement that in cases of minimal displacement internal fixation, either by a Smith-Petersen pin or three Moore's pins, gives excellent results, and where the displacement is considerable Vaughan-Jackson (1956) has shown that an attempt at reduction by gentle manipulation is justified.

The treatment of the irreducible displaced epiphysis is more controversial and I would like to support early correction of any residual deformity in such cases by a subtrochanteric osteotomy as opposed to cervical osteotomy. Brilliant results have been obtained by the latter method, but almost every series reported which has been observed for any length of time reveals an appreciable number of cases with avascular necrosis of the femoral head. It has been argued that these cases are the result of a failure of technique, but operations on the neck of the femur must always hazard the blood supply of the femoral head. On the other hand, correction of adduction and external rotation deformity by removing a wedge of bone from the outer side of the subtrochanteric region results in a stable, painless and relatively mobile hip-joint. Following operation it is our practice to immobilize the hip in wide abduction, and I feel that some medial displacement of the shaft is probably an advantage (Fig. 2).

Osteoarthritis of the hip-joint.—The typical case is a patient of late middle age with a great deal of pain, but often a surprisingly good range of movement, who frequently exhibits signs of degenerative changes elsewhere. In such cases we have found arthrodesis difficult to achieve and the operation a severe tax on the patient's endurance. With a few exceptions the use of a prosthesis has been disappointing, the joint gradually deteriorating two or three years after the operation, with the return of pain and instability.

McMurray's displacement osteotomy has, on the other hand, continued to give consistently good results. In a fit, relatively young person, post-operative immobilization in a plaster spica is probably the ideal treatment. Internal fixation has undoubtedly widened the scope of the operation, and the ability to get patients up on crutches at the end of three or four weeks certainly makes it more attractive (Fig. 3). The technical difficulties of adequate

←FIG. 3. — Bilateral displacement osteotomy for osteoarthritis of the hip-joint using a straight blade plate for internal fixation.

internal fixation should not be minimized. Whatever method is used the greatest care should be taken (1) to see that the appliance does not hold the fragments apart—it should in fact allow impaction to occur, and (2) to see that the limb is in the proper position before the plate is finally screwed to the shaft.

Those of us who have practised this operation for many years can, I think, honestly say that it has provided us with a higher percentage of grateful patients than any other orthopædic procedure advocated for this condition.

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The Treatment of Cervical Fractures of the Femur [*Résumé*]

By R. S. GARDEN, M.Ch.Orth., F.R.C.S.Ed.

Preston

and W. R. D. MITCHELL, M.Ch.

Northampton

Mr. R. S. Garden: The operative treatment of cervical fractures of the femur was discussed against the background of the anatomical and functional features of the femoral head and neck. Adequate reduction was considered to be the essential preliminary to any form of treatment.

The internal weight-bearing system in the proximal end of the femur was believed to be compressive in nature, and the main load direction was shown to run in a steep line within the head and neck. It was felt that internal fixation should respect this system if both weight-bearing and the maintenance of reduction were to be achieved.

The results of treatment in a series of 137 patients who had been treated by means of the low-angle Küntscher nail over the past five years were examined. 36 patients who sustained incomplete, mid-cervical, basal or intertrochanteric fractures, and who had survived a three-month period, all united without deformity. Of 56 patients who had sustained fully displaced subcapital injuries, and who had been followed up for at least twelve months, 75% had united well. Further examination showed that union had followed in almost every case in which good reduction had been achieved, whilst poor reduction had invariably resulted in ultimate failure. In the presence of unsatisfactory reposition of the fragments, therefore, the use of low-angle fixation with early weight-bearing was to be regarded as a worthless procedure.

Mr. W. R. D. Mitchell: My first point is a plea for early weight-bearing. Most of these patients are over 70 years of age and six or twelve weeks off their feet leads to other complications. Unfortunately the neck of the femur is angulated in relation to the shaft and as in the angulated fracture of the tibia weight-bearing leads to nonunion. By a suitable pinning technique, however, varus can be reduced or eliminated and the intact calcar femorale of the shaft brought medial to the point of weight-bearing on the femoral head. Weight-bearing now results in impaction which we are all agreed is desirable, and I believe it is most important in the first three weeks following fracture.

My technique now is to reduce into a valgus position if possible and impact heavily before inserting the guide wire when the femur is exposed. A low nail resting on the calcar femorale is inserted, but if it has not been possible to reduce the fracture so that the calcar femorale of the shaft lies medial to the point of weight-bearing of the head, a subtrochanteric angulation osteotomy is done after a wide-angle Jewett nail plate has been inserted low in the neck. After operation the patient is got out of bed as soon as possible and is taught to stand on a wide base holding on to the end of the bed and swaying from side to side. In a day or two walking with full weight-bearing is encouraged, at first with a wide base.

In our series avascular necrosis in a group treated by this method was about 4% compared with 9·4% in the rest, but the group was too small to draw conclusions.

In our analysis we tried to reconstruct the spatial relationships of the fractured surfaces. We have the impression that about 25% of cervical fractures fell into a group where there was appreciable "coning out" of the femoral neck. It was in this group where we encountered most trouble.

I suggest that early ambulation with a low-angle nail as described by Mr. R. S. Garden gives better and not worse results than treatment where weight-bearing is delayed. More frequent use of the angulation osteotomy for certain types of fracture is advocated.

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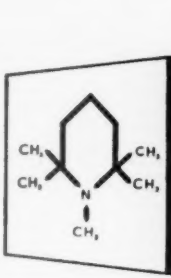

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Section of Psychiatry

President—ELIOT SLATER, M.D.

Meeting
May 12, 1959

SYMPOSIUM ON SEXUAL PROBLEMS IN MARRIAGE

Dr. H. V. Dicks (London):

Psycho-Dynamic Aspects

The fact that this paper is with others of a very practical and empirical nature, suggests a continuing gap in our psychiatric world between practice and concepts. On the one hand is the assumption that the failure of a physiological function is a condition in its own right that only needs to be restored in order to re-adapt or adjust a person who has such a "symptom". On the other hand, there is the assumption that behind the failure of the organ function (the symptom) lie emotional drives which block or deflect the process which in health allows that function to unroll and fulfil itself smoothly. In other words, the symptom is not the centre of interest. Nobody now treats fever as such. Both sides can accept the concept of a conditioned reflex as one level of explanation. The non-analyst will perhaps seek to "re-condition" the response by conscious training, or by suggestion, fortified by some physical agency or instrumentation. The analyst will tend to seek out the forces antagonistic to the healthy process in the mind and attempt thus to under-cut their dynamic interference with the progress of the healthy drive to its bio-psychological goal. The analytic psychiatrist is thus primarily interested in understanding the meaning of a symptom in the economy of an individual's adaptation to his reality and to the demands that reality makes upon him.

It is now a commonplace of this way of thinking about mental phenomena (and their physiological manifestations) that the most important reality to which individuals have to relate are other human beings. It is assumed (1) that all human beings are goal-seeking; (2) that they are impelled to make relations with objects that promise the satisfaction of these goals; (3) that the capacity for making such relationships is liable to interference by other goal-seeking drives, which may also be connected with the same object, thus setting up stress.

So far, this statement of the analytic position *vis-à-vis* symptoms of neurotic dysfunction is applicable to all the phenomena covered by the hypotheses of *intra-psychic conflict* and of *ambivalence*, widely accepted as well-founded on observed clinical data.

The dynamics of the marital relationship and its disturbances.—The marital relationship is a special, indeed unique, relationship within the above broad context. It is a voluntary, mutual undertaking to satisfy each other's biological and emotional needs for close intimacy and interdependence to a tolerable degree within the framework of social sanctions of the society of which the spouses form part. Implicit, and often explicit in the minds of the partners, is also the goal of forming a new social integrate—a new family, with its own distinctive internal culture derived from the blending in various proportions of the personal resources of the two partners. Thus, we can conceive of the marital relationship as an *interaction* of two persons at conscious level, as well as a more unconscious "transaction" (Spiegel, 1957) of unrecognized forces in two persons with a long developmental history: persons now required to play social roles—of spouse and later of parent—in accordance with the perceived needs and values given to such roles of self and other, but always within the limitations of the cultural and personal values and capacities each brings forward from the past, and which, to some extent, also determine the potentials for congruent maturation and change possible for each partner within the relationship.

It follows that in the study and appraisal of any disturbed marital relationship, we have, after elimination of organic disorder or deficit, to take account of possible conflict in this role taking and role expectancy of "self" and "other" at three levels: (1) intra-personal; (2) inter-personal and (3) explicit socio-cultural.

(1) *Intra-personal conflict* in each partner's make-up. The capacity for, and personal interpretation of, roles which each will bring into the marriage is in large measure an outcome of the learning process in object relations with significant figures of the dependent childhood phases and the conflict inherent in this succession of inevitably ambivalent attitudes. It is on the outcome of these earlier nuclear experiences in object relations that the fate of later capacity for libidinal and personal maturation and competence to the level of innate potential depends. The child is father to the man, so to speak. The personality is nourished by the assimilation of loving feelings; is stunted and distorted by their lack. It cannot give out what it has not taken in,

or expects to receive back. Learning to be an adult is a function of love. If this is broadly true, then the presence of violent ambivalence or fear experienced and not overcome during the dependent childhood phases, will prevent or interfere with subsequent living through the needful sequence of the developmental process. The individual remains deep down still at grips with the objects of the conflictful situation—usually a parent or sibling figure. We thus have to assess each partner in a marital problem in terms of these nuclei of fixation and of the typical defence mechanisms guarding them: hysterical dissociation and denial; splitting of his objects into good and bad; projection; or depressive anxiety, to name but a few commonly observed postures which characterize the attitude and role performance of each partner towards the other in disturbed marriages. I am speaking here not of mentally sick persons in the ordinary sense, but of reactions to the spouse only. It may be of interest here to state that in over 95% of a sample of 157 marriages seen at the Tavistock Clinic we found a history of broken or grossly disturbed parental marriages, while a normal control sample showed 54% of these factors.

(2) This leads on to the *second level* of study—one perhaps most typical of the kind of work my colleagues and I have been engaged on in trying to diagnose and understand the varieties of marital tensions.

At this level, one is concerned with the "transactions" between the two "internal worlds" of the spouses, what they seek to do to, or get from, each other at more or less unconscious depth. Instead of the healthy integrative congruence, or "fit" of a normal marriage, the partners in a "sick" marriage are in an unwitting way discharging on each other some now re-projected part of their conflictful former object-relations. I stress *on each other*. Feelings such as frigidity or sulking or withdrawal are always about somebody else, even if that somebody else is, in part, an Aunt Sally for an internal object. One is never impotent or excited except in relation to another, even if that other is but a masturbation fantasy. Even if we can assign to one of the partners a more obvious primary role, in importing into the relationship his or her fantasy-distorted and conflict-laden expectations or demands, the fact remains that the other was for too long emotionally predisposed to be blind to the signals from this deeper level, or denied them, or *chose the mate* in some way because of these. Regressive behaviour, moreover, tends to evoke latent ambivalence in the "healthier" partner who may, in terms of symptomatology of neurotic defence, suffer more obviously by the time the tension has reached the stage of asking for help. My point, then, is that the study of marital sexual problems is a two-body social psychology, a study of a dyad.

By way of examples of such a dyadic collusion, two recent cases may be briefly cited, because they illustrate the essence of the commonest marital situations we meet in our practice.

(*a*) Mr. and Mrs. A., aged 23 and 21, married eighteen months—seen because of wife's inability to permit consummation. Her history was of exciting, forbidden, love-play with young men whom her stern father used to chase off literally with a whip. When her husband appeared, the father accepted him at once as a "decent, dependable sort" and gave his blessing. The husband was indeed just such a young man, with another stern father who taught him the utmost deference and chivalrous solicitude towards his invalid mother who had spinal disease. The young wife, at single interview, confessed she found the husband too quiet and meek and unexciting and repeated this at later joint interview when she expressed the wish that he were stronger and that he ought to beat her for her stupidity. She had lost all interest in him as a sex-partner as he had not overcome her and was "too nice".

Here is a simple instance of what we have come to call "collusion": the wife's mate choice was determined by her guilt over her masochistic, "bad" sexuality. It was in contrast both with naughty boys who excited her and probably also with the strong, stern, whip-wielding father who could chase off any boy and knew how to keep girls in order—an object which alone seemed sexually desirable and worth "falling for". This is a very frequent conflict in the present-day woman. The stern father formed an *unconsciously shared image* of both partners: the husband was in conflict over his own aggressive drives towards women as forbidden by his "internal" father and interpreted his marital sexual role as that of a good, gentle little boy, probably because he projected his unresolved tie with his mother into his relation with his wife and conformed to the model of husband he had learnt from his historical father. So the wife's and husband's needs in respect of these more immature sub-systems or sub-identities dovetailed perfectly, to the detriment of their adult needs.

The husband still had erections, but effectively he was impotent and his wife had, to continue the metaphor, the whip-hand. Dilators and all the rest had been tried, only increasing her disgust with the whole thing.

(*b*) Another young couple of the same age group and duration of marriage showed in a sense the obverse picture of collusion. Both were only children and had in common a matriarchal background. The wife's model for

identification was a conventional mother with middle-class status aspirations and with a tame, mean father, by contrast with whom she chose a go-getting young rebel of working-class origin, himself torn by loyalty to his much-abused mother whom he defended and also depended upon, and the discouraging model of an unsuccessfully assertive, despised father who deserted the mother from time to time.

At one level the young couple met over this revolt from maternal envelopment. It would all be different with them. He was determined to be boss, and indeed socially and financially lifted himself quickly to a secure and promising position. But when his wife surprisingly continued to be friendly with her parents, and showed attitudes resembling her mother's, he began by resenting what he felt to be a female conspiracy to get him into the mother-in-law's orbit, and when the wife also became pregnant, he felt impelled to declare he would clear out. He did not do so because of his counter-identification against his father, but he began expressing all the hate of feminine demands on himself towards his wife with near-paranoid intensity and lack of insight, and went stone-cold towards her. Only his wish to protect his baby son from a similar fate, he feels, now keeps him at home.

The wife is quite incapable of seeing that she contributes to this by her unchanging expectation that somehow she can mould him to become the helpful, errand-fetching "bourgeois" man she saw her own father to be. The more she carries out this appeal to his chivalry, the guiltier and angrier and more obstinate he becomes, even though so far he intends to do better than his father and stay with his family. He is beginning to be aware of his deeper, repudiated, likeness to his father.

Even from these two over-condensed cases, we can make some hypotheses about the chief varieties of such collusive transactions, manifesting in disturbances of communication and sooner or later of sexual functions in spouses. Before generalizing on the basis of this kind of study of some 300 cases, as well as on the experience of the Family Discussion Bureau with its cases extending into thousands, I should like to mention the *third level* of analysis of the ætiology of marital tensions.

(3) This we may call that of the *explicit socio-cultural role expectations*, norms and values. This is, in one sense, the easiest and most traditionally accepted conceptual framework for interpreting marital tensions. It is implied in the anxieties of parents about the risks and dangers of their children marrying out of their race, nation, faith, class or local culture pattern; and there is indeed evidence that such culture distance is of some importance. My colleagues and I are in the habit of carefully enquiring into and comparing the expressed norms of role aspirations in marriage of the partners in relation to the norms and values of their respective backgrounds. We find that this is not a simple matter, either technically or conceptually. Not only are there numerous areas in which co-operation can either succeed or fail by reason of rigidly held differences in norms. We need to enquire closely into such things as values given to male/female role differentiation and dominance/submission, over the areas of finance, household tasks, child-rearing policy; demonstrativeness; relations with friends and kinship groups, æsthetic, political and social attitudes; religious precepts and practice, as well as narrowly sexual mores. We have also to allow that where these things lead to friction (whereas they were brushed aside or ignored during courtship), their emphasis during conflict may be due to the tying up of these values and sanctions with the persisting fixations to parents who imparted them, rather than due to belonging to a given society or culture group, and that the denial of these deeper differences was part of the collusive process of the "rebellion" against those parental norms one did not know one still cherished. Hence, the astonishing fact that a spouse may become impotent because the other has ceased to belong to the Communist Party, or no longer goes to the Congregational Church, or is a "square".

I repeat, the material forming the basis for these remarks is not drawn from the generally maladjusted. The Tavistock sample is mainly of the higher social and educational levels, with some 66% of I.Q.s at the level of 120 or better, and nearly 99% of professional, white-collar and skilled artisan levels, showing marked upward mobility, 71·6% declaring adequate or better economic conditions. They come to our Unit only because of marital stress.

Over-simplifying for the sake of brevity, we may divide our material into (1) those with overt sexual disturbances of potency; (2) those in whom sexual disturbance is relatively not stressed, and who emphasize some sort of incompatibility at social level, at times in painful contrast to the remaining sexual bond now felt as degrading, against which one or both partners may be in revolt. Here I shall sketch only a few of the variants in the first subdivision.

Some discovered patterns of sexual dysfunction in marriage.—Among the spouses coming to treatment because of overt genital failure, we have to distinguish those *who fail from the beginning* of their sexual relationship, from those where genital relationship deteriorates slowly or, at times, with

dramatic suddenness, to vanishing point, after being more or less successfully established and maintained over a number of years of marriage.

(1) *Primary sexual failure.*—This aspect was illustrated by the first case I quoted, though variants occur in both sexes, even in those who marry at relatively mature ages, where it cannot be put down to mere late adolescent immaturity. The essential constellation is nearly always, in our experience, the interaction of a man with more or less unconscious fear of the woman as a potential destroyer or persecutor, whom one therefore dare not attack, and a woman with a more or less unconscious conflict over taking a feminine reproductive role which is felt as threatening her "identity" as a person, perceived in modern terms as tied to a career or other quasi-masculine alignment. The sub-identity of the inwardly rebelling boy, who because of his fear is outwardly good and considerate, clashes with sexual demands of the biological reproductive drive of the male. In the female, the more biological need to surrender in the reproductive act clashes with all the variants of the shrew or the former tom-boy.[1] She will, in fantasy, yield to someone stronger in personality—a hero figure at first projected to the chosen swain—but she makes sure that, in fact, he offers no real threat and so he can soon become the object of contempt. In brief, there is apt to be sex-role reversal, at least in fantasy. Women are pretty good at spotting mere spurious pseudo-assertion in the man and will not let him forget it. Nature abhors a power vacuum. We can in passing here include the varying degrees of partial homosexuality in both sexes which march inevitably with spoilt, overmothered men and women, the results of our present small-family culture (Dicks, 1955).

It is in these cases that in the past one might have advocated analytic therapy for the more obviously incapacitated partner—or at least the one who first presented with symptoms. Orthodox analytic technique might have done quite a lot for the overcoming of the sexual neurosis in the individual. But the equally orthodox analytic policy of excluding the spouse or other relatives rigorously, was also likely to lead to divorce—because the important concept of unconscious collusion would have been left out of account. I will return to this point later.

The furtive and exciting courtship love-play is replaced by guilty constraint with the change in role perception and sense of commitment. The analogues of the fear of "giving oneself" for the two sexes are complete male erection failure and vaginismus respectively. Lesser degrees are represented by ejaculatio præcox or orgastic failure which represents an anxiety-laden compromise, and unpleasurable frigidity. Put in another way, the orgasm is in fantasy equated with loss of identity, giving oneself up into another's power; the whole act is equated with dangerous aggression, derived from infantile fantasies based on the experiences of parental strife—what Freud called the "primal scene"—and its attendant horrors. This unconscious ambivalence projected mutually is often covered by the statements and beliefs of great happiness "in all other spheres" of the relationship. Here we have to distinguish two variants again. In one variant—and this applies to both sexes in fantasy, but to males more frequently in overt behaviour—there is the so-called libido-split. Potency or capacity for genital function of a sort exists in relation to partners thought of as debased: prostitutes, coloured women abroad, and so forth—or the "bad" boys in the wife in our first case—where dependence and commitment are minimal, and the act has an aggressive or defiant flavour. Potency is inhibited in relation to "the sort of person one marries", because that person is idealized and de-sexualized, being thus protected from one's guilty and destructive inner fantasies surrounding sex, equating it with excretion or greed. In other situations it is the disappointment, when this idealization is destroyed by the partner actually making sexual demands, which begins the process of projection on to him or her of one's own split-off or repressed sex needs. The ambivalence is, so to speak, turned inside out and persecution and revenge now break surface.

(2) *Secondary sexual failure*—the much more complex subject of those marriages in which sexual functions die out, with varying degrees of hostile defensiveness, at some period later than an arbitrarily defined period we could call "the adaptation period". We find that the largest fraction of our patients are in their fourth decade and have on an average been married eight and a half years. The Registrar-General makes the same discovery in his 1954 Review, but the duration of marriage at the time of divorce in his figures is 12·8 years. The age groups over 50 form the largest fraction of the total married population, but these are only 2·6% of our sample, although accounting for 13·9% of the divorces (1954).

In these late cases of sex failure in marriage, the picture is rather different in its surface manifestations. The emphasis is on general incompatibility of personality, with the change just described for primary cases taking place in the inverse manner. The idealization dies more slowly and is referred to areas other than the sexual one. One might say that the sexual drive

[1] *Vide* Leopold Stein's "Loathsome Women", just published.

and its attendant child-rearing co-operation are often the last bastions of the relationship to crumble. It is only in a part of our cases where a libido-split, operating the other way round, had caused at least one of the spouses to marry mainly for sexual attraction without much else that fitted, and long-range boredom and lack of common interests do the damage. Some, especially, of the marriages contracted when very young have seemed to be of this kind. In the greater part it might be said that it was certain deeply held and cherished expectations that the partner and oneself could play their role in accordance with a fantasy model one carried inside, that were disappointed. The partner or one's own needs were not seen realistically. The defensive rigidity and incapacity for changing one's demands or one's view of a real person seem then to lead to the vindictive withdrawal symbolized in growing sexual coolness and finally impotence. It takes some years for the defensive idealizations to wear thin. It is only feasible to sketch some typical variants, without in any way claiming that these are rigorous sub-classifications or syndromes. It is too early to think in these terms.

Winch (1958) has ventured into classification. Firstly, we can readily see the marriage which flourishes for a time on the *Pygmalion* pattern. It is the fate of Pygmalion to suffer the results of his own narcissistic, patronizing and often sadistic infatuation with bringing the statue to life. When his Galatea matures, she shows all the ambivalence of her previous worship of the superman-father figure. Either sex can in clinical experience be found in this role, moulding the partner in accordance with the unconscious model—most often their own idealized parent.

Then—there is the Ibsenian father-daughter (baby, doll) variant, and the mother-son variant —often coinciding in the same couple: each wants the other to act as parent-substitute, making demands, but unable to give much adult security or love. Winch next describes a *Thurberian* type of marriage, in which the wife is the product of a dominant mother whom she has rejected, hence she looks for a good, unassertive mother-substitute in her husband, yet is also identified with the mother as the despiser of weak, submissive men, who, in turn, seek out such a mate because she fills the need for just such a dominant mother. In people of our sample—the more intelligent and perceptive—it evidently takes quite some years for these underlying mutual fantasy-projections to exert their effect. Sometimes it is the motherhood of the wife which begins the process in both partners, sometimes the unequal maturation which ends the success of the collusive process, revealing the latent ambivalence.

In some of the couples the tensions are but episodes akin to growing pains which may, at least in earlier stages, end in reconciliation and in a great access of tenderness and sexual activity. But even in them the episodes are marked by a conscious diminution or extinction of sex feeling for the partner. The point is that when the marriage is one in which the partners are unable to tolerate ambivalence and split it instead into its component feelings, the genital libido for each other is thereby greatly weakened. Every couple examined reports such disturbances.

Sexual coldness follows closely upon the rift. From the moment when the disappointment of role expectation begins the process, the regressive corollaries become activated, unconsciously influencing the pathways of "somatic compliance" —the sexual function. It could be said that when the marriage partner becomes fused in fantasy with the idealized and yet frustrating parent figure, the incest-barrier is conjured back to life in relation to them. Guilt and anxiety are the enemies of Eros, for they are always the defence reaction against aggression in fact or fantasy, from within or without. At times they can be smothered by an aggressive, loveless sexual life from which tender, giving elements are absent and by which the partners feel debased rather than exalted.

Some observations on therapy.—The group with which I am associated has, as the result of its long experience in marital diagnosis and therapy, come to hold the view that interpretative therapy on the basis of psycho-analytical and allied hypotheses carried on in parallel on both spouses offers a most promising and relatively thorough-going form of help to the many varieties of marital failure. The work is carried out on a once-a-week basis by one therapist for each spouse operating as a team, with frequent conferences.

In marriage which has not deteriorated to the point of irreversibility, this paired technique (perhaps ideally by a male and a female therapist) is capable in a relatively short time and at low specialist investment of yielding rewarding changes towards maturity, to diminution of fantasy-determined role conflict and role expectations, and an increase in reality perceptions of the partner's needs and personality, including frustration—and ambivalence-tolerance. The pitfalls of heavy transference involvement or of acting-out are obviated because with both spouses under treatment the transference interpretations are always related back to the marital situation where in such conditions all kinds of new ways of behaving can be tried out in safety—including flaming rows. As stress of conflict and hostility decreases, so sexual functions are recovered rather naturally.

This form of treatment requires pretty full assessment of the individual as well as the dyadic potentials of the partnership. For this, in addition to long individual interviews, we have begun to elaborate some new tests. As may be known from my previous publications, we have also made extensive use of the joint interview—mainly for interaction diagnosis, but also experimentally for therapy, used repeatedly.

These forms of therapy endeavour to use the very forces which created the conflictful but still potent bonds in the collusive marriage, because in them lie latent the stifled needs pressing for satisfaction. If such bonds have never existed, or have atrophied to the point of no return, then nobody could help except the divorce judge. It is after divorce that individual analysis has a place—to prevent the individuals concerned from repeating the same pattern a second or third time. We have had occasion to study such "repetition" in our Unit.

In conclusion, rather than attempt to present a list of the varieties of sexual dysfunctions and their specific psycho-pathology, I have chosen to speak at a fairly abstract or general level in order to stress the beginnings of a conceptual rationale for the kind of treatment developed by the Tavistock Clinic Group. This theoretical framework enables me to concede the therapeutic possibilities inherent in any good personal relationship in which the doctor is invested with the mantle of a good, permissive parent figure who sanctions sexual potency and initiates the patient into it. My guess would be that this form of therapy would work best in the early failures of adaptation due to near-hysterical inhibitions mainly culturally determined. If I have bewildered you, then I have succeeded—for let nobody think that much is firmly known about the dynamics of marital relations or that any one treatment is the answer. Indeed, sometimes our best treatment is to let sleeping dogs lie.

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Dr. G. L. Russell (London):

Impotence Treated by Mechanotherapy

The *coitus training apparatus* (C.T.A.) was introduced into this country twenty years ago by Dr. J. Lowenstein. It consists of twin splints of light metal encased in rubber, joined at the anterior end to a ring which encircles the *sulcus glandis*, and at the posterior end to another, larger, ring which rests on the *symphysis pubis*. Both rings are hinged above to permit the introduction of the penis from below. The splints are held in position by a rubber band linking the two halves of the pubic ring.

Each appliance is made to measurements taken on the flaccid penis, i.e. of the circumference (at the sulcus) and of the length from sulcus to symphysis.

It is of course essential that the patient's wife be prepared beforehand and co-operate willingly in the treatment. Dr. Lowenstein used to insist on seeing each patient's wife, explaining to her in detail how the C.T.A. worked, and disposing of any resistance in a magisterial way. This may not always be possible, though it is always desirable. Certainly it is a mistake to accept the husband's view, unsupported by further evidence, of what his wife will think of this form of treatment. The man who says he is "sure she'll have none of it" is more likely to be expressing his own feelings than hers. Naturally many women (as well as men) dislike the idea of a mechanical aid, and some fear it may hurt or injure them. As a rule they are quickly reassured. Of course not all will co-operate, but the failure to do so is evidence of an attitude to the partner, or to the sexual function, which would by itself be enough to ruin the marriage. Nevertheless, a few of the best results are obtained where most stubborn resistances have first to be overcome.

The wife is told how to introduce the penis, enclosed in the C.T.A., into her vagina, holding it between her thumb and forefinger and guiding it towards the *introitus*.

Perhaps it goes without saying that in many cases sheer ignorance of the physical parts and processes has been largely responsible for the sexual failure; and simple instruction in love-making is then a necessary part of the treatment. It is as well to assume—for the purpose of this education—that ignorance is complete, for otherwise one may easily omit (as too obvious to be worth mentioning) just that detail the couple do not understand, and on account of which they have been unsuccessful over and over again.

It is important to emphasize, to both husband and wife, that they are embarking on a course of *treatment*—or, as Dr. Lowenstein preferred to call it, *training*—designed to help them achieve a satisfactory sexual relationship. The aim, in this first stage, is to learn a technique, not to experience pleasure. Naturally they will find satisfaction in being able to do, with the help of the C.T.A., what had proved impossible without it; but, to begin with, neither may reach an orgasm; or else the husband who has previously suffered from *ejaculatio præcox* will find that he still, while using the C.T.A., reaches his climax too soon. What mechanotherapy can ensure—and *all* that it can ensure—is that a couple previously incapable, by reason of the husband's impotence,

of having intercourse at all, can have it at will, at any rate in the sense that the husband can penetrate whenever he makes the attempt, and can prolong coitus as he and his wife desire, whether he reaches orgasm or not, or (if he does reach it) as long as he likes afterwards. The C.T.A. does *not* infallibly secure an orgasm, nor does it guarantee pleasure, for either partner. *It enables the man to penetrate* even without an erection—i.e. it enables him to perform the act which (more than orgasm) represents potency. And because it does this, it begins to reverse the vicious spiral of failure, humiliation, and anxiety which is, in the great majority of cases, the effective cause of impotence. This secondary anxiety (i.e. anxiety arising out of the symptom itself) must be dispersed before the natural mechanism can function naturally.

Once treatment with the C.T.A. has begun, the patient is enjoined not to attempt coitus without it. This is a necessary prohibition, for one of the commonest misconceptions about mechanotherapy is that the purpose of the splint is to "strengthen the erection". If not carefully instructed, many patients who find that they can penetrate with the help of the C.T.A. soon attempt to do so without it, find that they cannot, and conclude that the treatment is a failure. They have to be told, emphatically and repeatedly, that they must forget all about the erection and concentrate simply and solely on learning how to have intercourse with the help of the support. Unless they do this, no improvement is possible.

Dr. Lowenstein made it a rule that no patient should attempt to have intercourse for a week after being supplied with a C.T.A., and should spend some time every day teaching himself how to apply the support accurately and quickly. At the end of the week, he must be able to satisfy the doctor as to his proficiency before receiving permission to proceed. I do not insist on this rule, chiefly because very few patients will keep it, and in many cases it is unnecessary. But one must, of course, make sure that the patient has learned the drill properly; though with very clumsy, or anxious, men this takes a good deal of time, tact, and patience.

The patient is seen again in a week, or at most a fortnight, partly because mistakes in using the C.T.A. need to be corrected at once if the patient is not to lose faith in the treatment, partly because, without some encouragement at this stage, the result—even when the proper technique has been followed—may be disappointing, and both husband and wife inclined to "give it all up".

Complete success, at this early stage, is not uncommon. Any of you who have used this treatment will remember the broad grin and exuberant air of the man who, perhaps for the first time in his life, has been able to penetrate, to experience an intra-vaginal orgasm, and to content his wife—all by the same operation. Early success is of good prognostic omen; the patient may be expected to be able to dispense with the C.T.A. in a month or two, if not sooner.

More often the patient, when he attends for the first time after using the C.T.A., wears a different mien. Yes, he and his wife have tried it—but it wasn't very successful. The support "slipped off"; or he couldn't penetrate properly; or it hurt his wife. He didn't have any "feelings"—of desire or pleasure; or (perhaps the most frequent complaint) "it didn't give me an erection". Various impediments are invoked to explain why they have not tried again: "I had a cold—it was the wife's period—I was tired." Here we begin to encounter the conflicts which are ultimately responsible for the impotence: deep-rooted hostility and dislike which have found only this means of expression, or guilt and inferiority manifest in the rest of the patient's life.

Between these two extremes—those who succeed at once and never look back, and those who have no genuine wish to succeed—are the group of patients who have (or may reach) a good relationship with their wives, who are not fundamentally disillusioned or defeated (except about their ability to perform the sexual act), but who need a great deal of encouragement, perhaps for several months, if they are to make the best use of the treatment. I think myself that psychotherapy (if one may call it that) should in these cases be limited to that amount of explanation, advice and support which is necessary to get them to persevere with the C.T.A. technique. It is a mistake to let oneself be drawn into elaborate interpretations. When a patient asks me: "What is the cause of my impotence?" I tell him I do not know—which is nearly always the truth. Nor, as a rule, do I attempt to find out. I disabuse him of any mistaken notions he may entertain—that it is due to organic disease, masturbation, injury when he was young, or the small size of his genitals. For the rest, I say it is more important to put things right than to know why they went wrong.

This will seem a quite indefensible attitude to many, perhaps to most, analytically trained and orientated psychotherapists. As one who spends most of his time doing psychotherapy, I can only say that it seems to me justified by its results. Naturally quite a number of C.T.A. patients have received psychotherapy—sometimes for several years—before I have seen them. Some of them have benefited considerably, in a number of ways. But it has not cured their impotence: if it had, I should never see them.

Results.—It is difficult to assess, and present, the results of this treatment accurately, for several reasons. Follow-up is unproductive, since patients who have not benefited cannot be bothered to answer enquiries, and patients who have been cured do not wish to be reminded of a period in their lives which is associated with so much misery and distress. Failure to reply to letters or keep appointments may as well mean success for the C.T.A. as the opposite. One patient, whom I saw only twice, and who neither returned to hospital nor answered my letters, sent a Christmas card to the doctor who referred him for mechanotherapy on which he had written: "It *works*!" This is the only evidence I have about the result of his treatment: it seems sufficient.

Failures, of course, may be concealed as well as successes. A patient whose aggression is so inhibited that he cannot tell the doctor the treatment is no good, may invent quite plausible accounts of his sexual progress. But these are belied by his demeanour, and will be refuted by his wife.

Thirdly, because impotence is not uncommonly a sign of some transient situation of strain or insecurity—such as a failure in business—it may disappear when, and only when, this situation has changed. Treatment, whether by C.T.A. or other means, has not affected the issue—though it may seem to have done so.

Review.—Of 66 consecutive cases treated at the St. Marylebone Hospital, 17 (26%) were cured by mechanotherapy—i.e. the sexual function was restored so that normal coitus, without the C.T.A., became possible. (More than half these patients had never been potent before.) The term "normal coitus" is perhaps ambiguous. It is here used of all those patients who, unable to penetrate because of deficient erection, were after treatment able to do so at will, without mechanical aid. In some, penetration was not, or was not always, followed by orgasm; but since the symptom which had prevented intercourse altogether had been abolished, these patients were included among those cured.

In 33 (50%) treatment resulted in regular coitus by means of the C.T.A. For some, coitus was possible—but less satisfactory—without it, and so its use was continued.

In 16 (24%) the result was failure, usually because either husband or wife would not persevere with the treatment, or with the marriage.

If so-called "involutional" impotence is excluded, in only one of these 66 patients was there evidence of any organic disease responsible for the symptom.

Type of onset.—In 9 cases (14%) the onset was *sudden*, and in 23 (35%) *gradual*. 34 (51%) had never been potent either before or since marriage—a period of ten, twelve, fifteen, and in one case twenty years. A sudden onset following injury, illness, accident, or the wife's confinement, often represents the crystallization of an unsatisfactory marital relationship, the "cause" being little more than a thinly-veiled excuse to "give up trying". It is probable that a more searching enquiry would establish that most of the patients alleging a sudden onset were becoming gradually less potent up to the time when the illness or accident said to have "caused" their impotence offered a way out of some matrimonial dilemma without the need to face all its implications.

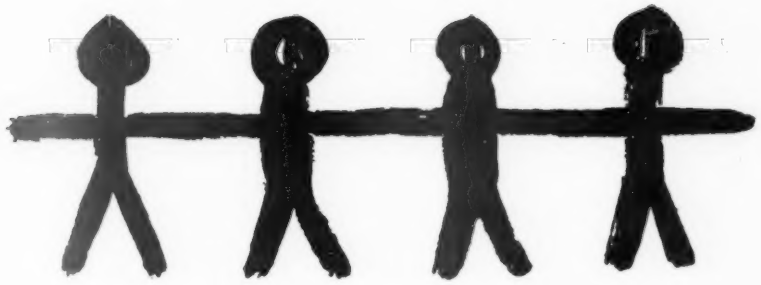
It is found in practice that *testosterone* has no decisive effect on the course of treatment. Most of the patients in this series had had it prescribed by one route or another, before they came to my clinic. A few said it had improved their erections, most that it had had no noticeable effect, none that it had made penetration possible when it was not so before.

It is sometimes suggested that mechanotherapy is a purely technical device and that C.T.A.s might be distributed by instrument-makers or some other agency, not by doctors at all. This is mistaken. It would be no more justified than to allow dental plates, for instance, to be purchased over the counter, to be used, misused, or not used at all by the customer. While no systematic psychotherapy is attempted in conjunction with mechanotherapy, the treatment must at every stage be backed by encouragement, explanation, and persuasion: without these the proportion of failures would be far higher than it is. Minor adjustments of the apparatus have to be carried out in the early weeks of therapy; and faulty techniques—and wildly mistaken ideas—of the sexual act tactfully corrected. All this demands a proper clinical setting, the support of frequent interviews during the early stages, and, in the more intractable cases, contact for many months. A man who has been impotent for years is only too easily convinced that nothing at all can be done for him, and only too prone to abandon treatment as soon as something goes wrong. The proper place for treatment of this kind is the hospital or consulting room. Although it does not profess to go to the roots of the disorder and explore the emotional conflict, it offers relief to many men who have proved in their own experience that other forms of therapy are for them of no avail.

The following paper was also read:

Some Sexual Disorders in Women.—Dr. CARICE ELLISON (London).

The subsequent discussion was opened by Dr. T. P. REES.



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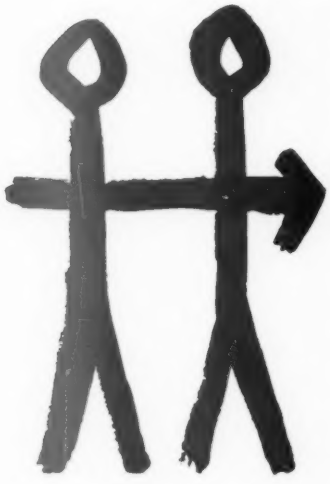

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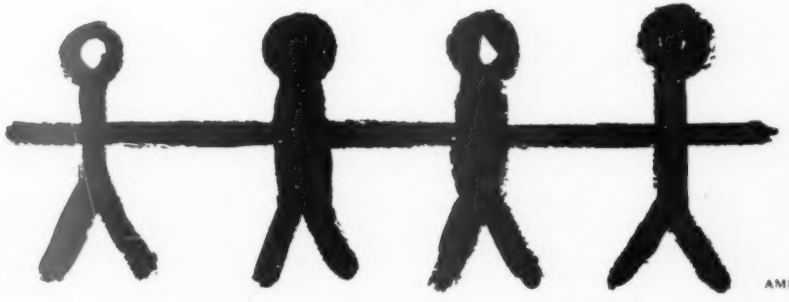

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Section of Medicine

President—A. H. DOUTHWAITE, M.D., F.R.C.P.

Meeting
March 24, 1959

DISCUSSION ON THE MANAGEMENT OF PROLONGED UNCONSCIOUSNESS

Professor E. A. Pask (Newcastle upon Tyne):

The Maintenance of Pulmonary Ventilation

Coma is an anæsthetist's business, but I do not think we are concerned here with therapeutic coma. The patients in coma from poisoning, injury or disease with whom I have helped have naturally been those in whom respiratory inadequacy was suspected. This can fit into the general picture of the sickness in various ways. (1) The insufficient breathing may be specifically caused by the disorder which has also brought about the state of coma, for example, cerebral hæmorrhage involving the medulla. (2) The respiratory neurons may share in a non-specific way in the low level of excitability which seems to characterize the nervous system as a whole, in most forms of coma. There is now experimental evidence to confirm this well-established clinical impression. It seems that most conditions which block the flow of sensory impulses into the commerce of the central nervous system will probably also lead to a diminished excitability of the respiratory neurons; they may then respond less actively to chemical stimulation. It may be that proprioceptive impulses are of particular importance in this connexion. (3) The bad breathing may be due to a mechanical accident incidental to coma. Food, saliva, regurgitated intestinal contents and so forth, may have been inhaled into the air passages. The immobility of the patient and his diminished likelihood of coughing may have led to bronchial blocking and pulmonary collapse. Coma is also often associated with poor circulation, with all its consequences for efficient breathing. (4) The poor breathing may be wholly or in part the cause of the coma. The bad breathing may be due primarily to mechanical or pneumatic causes, perhaps to a chest injury, neuromuscular disease, or an acute infection upon chronic bronchitis. The poor breathing causes a disturbance in the internal electrolyte and gaseous environment and, if this is severe, it often leads towards coma. I find it difficult to go farther than this, for though we can identify certain important factors which obviously go wrong when breathing is ineffective, I am not sure that we can yet say, with certainty, which of these factors lead the patient into coma. (5) The respiratory defect may in some way be a result of the state of coma. When the breathing defect becomes sufficiently severe, it may cause a deepening in the coma. If this happens we usually try to counteract the defective breathing and I think we should do so, but, though the coma may lighten as a result, the patient does not necessarily immediately recover consciousness.

When I am asked to see a patient in coma from disease I am often in very grave doubt whether or not the breathing is sufficient. The reasons for this uncertainty are many. The respiration may be very abnormal in its muscular balance or in its rate and rhythm. The physical signs elicited by auscultation, percussion and radiology will tell us something of the nature of the trouble, if it be due to disease of the chest, but they do not help me much to decide the important question of whether the functional defect is severe enough to menace life or to be regarded as a significant cause of unconsciousness. Cyanosis, which we regard as a certain sign of respiratory defect, may be strangely difficult to detect with assurance and, of course, its absence does not mean that breathing is sufficient. Then there is a curious difficulty which I think arises from seeing the patient too often and too long. These difficulties are illustrated by the following case.

A woman had been admitted to hospital with a diagnosis of virus pneumonia. For four days she remained alert. On the evening of the fourth day her breathing became jerky and irregular and finally failed as she fell into coma. Endotracheal intubation was easily performed and she was manually ventilated, using a bag and Waters canister, through the night. Next day the attending physicians thought that she needed tracheostomy and artificial ventilation. Though some spontaneous respiration was present, it seemed to them insufficient to secure oxygenation unless she breathed pure oxygen. She was still comatose.

There seemed no doubt that the initial loss of consciousness owed something to the respiratory failure, but was her coma now due to bad breathing only, or was there some other cause as well? Her respiratory exchange looked to me sufficient. Because she had dry crusted lips, labial herpes and seemed a little jaundiced, I simply did not know whether she was cyanosed when breathing air.

I think this kind of situation is not uncommon and we very much need the firm evidence of direct tests, but they must be quick and simple

enough to use in the ward, if they are to be of real service to our patients. In Newcastle, we measure ventilation with a very simple book-form spirometer rather similar to that of MacKesson. Ours is made from polyvinal chloride plastic sheet. Its disadvantage is that though it is easy to wash, it cannot be sterilized by heat. If the risk of infection seems high, therefore, we arrange that the patient shall breathe in and out of a polythene bag contained within an airtight bottle. The cavity of the bottle then communicates with the spirometer. The polythene bag is a sandwich bag costing a few pence and is thrown away after a single use. Now, whatever any of us *thought* about the patient's breathing, her ventilation was soon established as more than 9 litres a minute and when a little carbon dioxide was given her breathing increased notably and she soon demonstrated to us a tidal volume of considerably more than a litre. This was information, but not enough. For some years now we have been using the technique of Plesch (1909) for obtaining a sample of gas in carbon dioxide equilibrium with the mixed venous blood. About a litre of oxygen in a bag is simply rebreathed, for something less than the main circulation time. We repeat this after an interval, usually three or four times, using the same sample of gas which has already reached partial equilibrium. This method has recently received support from Dr. Moran Campbell. Having about a litre of gas, we try always to save some for accurate analysis but at the bedside we expel some of the gas through a bubbling device into an indicator solution buffered with bicarbonate, a technique I first encountered in the work of Jones and Griffith (1944) though I feel sure that it is much older than this. We use a set of colour standards for bedside reference. Within minutes we knew that the carbon dioxide tension in the mixed venous blood was not more than 52 mm.Hg, and therefore that the arterial carbon dioxide tension was almost certainly not above 47 mm.Hg.

Arterial oxygen saturation we still determine upon a sample of blood obtained by arterial puncture. We analyse it by one of the many variants of Kramer's original photometric technique. Our own peculiar variant has only the virtues that it is quick, needs a small (1 ml.) sample of blood and uses a relatively cheap colorimeter (Molyneux and Pask, 1955). This estimation was done and the arterial oxygen saturation proved to be 97%.

Advances in medical procedure should not be judged by their effect upon the doctor's emotions and perhaps I am here giving too much weight to my own peace of mind. Nevertheless, I do believe that by giving us a surer basis for action, the people who have developed such simple and practical tests, and those who have taught us to interpret them, have made some of the most significant advances in this field in the last few years.

In the particular case I have been describing I felt, as a result of the tests, that the coma could no longer be attributed in any very important degree to the defective breathing, that no tracheostomy should be performed, that the endotracheal tube and artificial ventilation had done their good work during the previous night and could now be removed. It turned out that this view was a profitable one for the patient.

If we find an important defect of breathing several questions immediately arise. First, can the defect be corrected by any artificial means available to us at present? If it can be corrected artificially, is there a real prospect that the natural functions will return and take over from the temporary artificial support? Under artificial means of the support of respiration we must include not only artificial respiration but all the physical measures which may be used to clear the air passages and reduce respiratory dead-space, as well as the administration of oxygen and of analeptics. There is no doubt that the benefits of tracheostomy alone provide sufficient assistance for some patients in respiratory distress.

My own interests have, however, been in the field of mechanical ventilation of the lungs. We have tried to concentrate our efforts on two types of respirator machine: those which can quickly be constructed and can be activated by a vacuum cleaner in an emergency, and those which are modest in size, cost and noisiness and which operate from an oxygen cylinder with a gas flow of less than 2 litres a minute. They can be used in the operating room as well as in the ward. We have tried to bear in mind the needs of the smaller and less well-endowed hospitals.

The general question might be phrased thus: "We have established that the patient suffers from bad breathing. If we could artificially improve this temporarily, would this contribute to the patient's ultimate recovery or remission?" Sometimes this question can be answered from a knowledge of the natural history of the disease, but one is not always by any means certain of the full diagnosis when the decision has to be made. I think all would agree that in the crises of myasthenia gravis and in polyneuritis, temporary artificial aid to breathing *does* help toward remission. In other conditions we are still uncertain. For example, in the bad breathing and consequent coma which may occur when an acute infection supervenes upon chronic bronchitis, I still feel uncertain how often, or in what type of patient, temporary artificial respiratory aid can contribute to real remission.

One reason for this uncertainty is that we have not always been whole-hearted in our attempts, so that the conclusion we drew from a particular case has to be indefinite. If we are to learn with certainty, we must create conditions in which temporary correction of the breathing defect can be achieved with certainty; or else that we shall surely know that we did not manage to do so. This may involve at least partial paralysis of the patient's own breathing muscles by relaxant drugs and it may involve also a willingness to apply necessary sedation when recovery of consciousness begins. In other words, it may be possible to secure adequate ventilation for the patient if he will drift with the tide and submit to the mastery of the artificial aid. If, however, he continues to attempt to breathe himself, the interaction of the patient and the procedure may result, not in collaboration, but in conflict.

Naturally, we hesitate to undertake such drastic measures. They make heavy calls on medical and nursing effort, and the present policy of reducing the real resources available for running our hospitals may make them impossible. Again, such elaborate procedures inevitably have their own complications and incidental hazards.

Most important of all, we fear that they might be an unjustified cause of suffering to our patient. On this last point I believe we may have been too sensitive. Surely we may take confidence from the immediate equanimity and, very often, the later amnesia of patients paralysed with myasthenia gravis or polyneuritis, who are given artificial respiration. Again, patients with tetanus who rightly or wrongly have been treated with muscle relaxants, artificial respiration and only light sedation, are not seriously distressed.

If we could establish in which circumstances and for which patients temporary, adequate, artificially-aided breathing could contribute to remission, then we should try to withdraw from such elaborate procedures and try to discover whether simpler measures would serve sufficiently.

In conclusion, when we deal with patients in coma whose breathing is bad, I think that making judgments is more difficult than taking action. We are especially indebted to the workers who have devised practical bedside tests of breathing efficiency and who have taught us to interpret them. There is much more work for them yet to do.

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Dr. Hugh Garland (Leeds):

The Treatment of Severe Tetanus

My position in discussing the treatment of severe tetanus in a symposium on the treatment of the unconscious patient is a little anomalous. Under no circumstances does tetanus produce prolonged coma, and such coma in a case of tetanus is always iatrogenic. Furthermore, when the patient with tetanus is treated by modern methods which produce total paralysis, we do not really know whether it is correct to say that he is unconscious, but many of the therapeutic problems which arise are common to those of prolonged coma whatever the ætiology.

My experience is entirely limited to that of the Tetanus Unit of the General Infirmary at Leeds; this consists of an anæsthetist, a bacteriologist, a general surgeon and a neurologist, the anæsthetist being much the most important member of the team. During the past four years we have treated 23 patients, drawn from a very wide area in the north of England. There were 18 males and 5 females, of various ages from 4 to 79. In 10 of them the causative injury was unknown, and in only 7 was the tetanus bacillus recovered. No patient had had antitetanic serum before admission and, as far as we know, none had been actively immunized. Since my remarks are to be restricted to the treatment of *severe* tetanus, severity must be defined; I shall use this term only for those examples of tetanus in which complete paralysis was induced. This was produced in 13 patients, the other 10 being treated by various sedatives, and sometimes by tracheostomy. I shall now describe briefly those indications which we have accepted as the necessary criteria for the use of this maximal treatment.

The commonest indication for inducing paralysis is severe tetanic spasms which can no longer be controlled by drugs, such as chlorpromazine and mephenesin. Rigidity in itself is not, in our experience, an indication; rigidity is a variable finding from one patient to another and from time to time in the same patient, often reaching a severity—in the neck, for example—which is never seen even in meningitis. Other indications have been depression of respiration from the use of sedative drugs, pulmonary collapse, hyperpyrexia, and obstructive vomiting after jejunostomy. The interval between admission to hospital and the induction of paralysis has varied from two hours to six days.

Our practice is to give antitetanic serum immediately on admission, and we feel this is especially important in those patients in whom the source of infection is unknown. At the same time our impression is that antitetanic serum only

prevents the further production of tetanus toxin, and there seems to be little or no evidence that it has any effect on established tetanus. It seems that tetanus is overcome by natural processes, in three or more weeks, and during this period treatment can only be aimed at keeping the patient alive. In only one case did we deliberately withhold antitetanic serum; this boy was treated with chlorpromazine intramuscularly for twelve days and was then transferred to another hospital for convalescence. Mild tetanus remained and about three weeks later he began to relapse to such a degree that complete paralysis became essential six and a half weeks after his first admission. We are still experimenting with the use of human serum from volunteers who have been actively immunized. At present there is no evidence that it is any more effective than horse serum but it eliminates the risks of anaphylactic shock, and the possible risks of producing jaundice are not considered to be serious. Human serum may also be of great importance as a prophylactic in a patient already sensitized to antitetanic horse serum.

Several drugs, all of the curare type, have been used for producing paralysis. We have abandoned Scoline, and we feel that all forms of intravenous therapy should be avoided if possible because of the serious and inevitable complication of venous thrombosis. We have recently used Laudolissin (laudexium methyl-sulphate) intramuscularly, the dose varying from 20 to 30 mg. The frequency of administration varies according to the severity of the tetanus, but is usually about two-hourly. The effect of this drug is to paralyse all voluntary muscle. It has no effect on the heart. During paralysis retention of urine and transient intestinal ileus are common, though there is no clear evidence that these are direct effects of the drug. When a patient is totally paralysed a serious problem arises as to his state of consciousness. Since he is entirely unable to express himself, it is impossible by any clinical means to know whether he is in any way aware of his surroundings. It may, in the future, be possible to make some assessment by the use of electroencephalography, but so far we have not found this to be a practical solution. The patient will, of course, have a tracheostomy, will be artificially fed either by an œsophageal tube or by gastrostomy, may have a continuous indwelling catheter, has to be turned with great frequency because of respiratory complications, and must be subjected to physiotherapy every few hours. Under these circumstances multiple cranial electrodes would present a serious mechanical problem. Even if this could be overcome, someone expert in the interpretation of the electroencephalogram would have to be available constantly. We have not found the solution to these problems. Since, however, the patient may possibly be aware to some extent of what is going on, it is our practice to use continuous sedation, usually with fairly large doses of paraldehyde given by nasal tube or gastrostomy (5 to 10 ml. every two to three hours). All we can say in defence of this is that every one of our patients has had complete amnesia for the whole of the paralytic phase of his illness. Whether or not this would be true if sedatives were not used must remain uncertain. It is our custom to give chlorpromazine in fairly large doses, with other sedatives, immediately complete paralysis is stopped, but we must admit that chlorpromazine introduces complications of its own. We have twice seen mild parkinsonism appear, though fortunately it has disappeared rapidly after this drug was withdrawn. There is another important complication of chlorpromazine in heavy dosage—namely that the drug must be withdrawn slowly, otherwise the patient may develop epilepsy. Before we were aware of this 3 patients had fits within a few hours of the withdrawal of chlorpromazine, and 1 went into status epilepticus. Fortunately there does not seem to be any tendency for epilepsy to continue after the first day or two. Sudden withdrawal must also be avoided, for the same reason, if heavy dosage of various barbiturates is used.

Full curarization must always be preceded by tracheostomy and followed by continuous positive pressure respiration. Tracheostomy has also been carried out when full curarization was not necessary, and in retrospect we think there have been other patients in whom this could have been done profitably; experience has also taught us that in some patients tracheostomy should have been carried out much earlier. 13 were subjected to full curarization, but we think that this should have been applied to 2 others, and should have been instituted at an earlier stage in 4. All patients, whether curarized or not, require constant attention. Areas of pulmonary collapse arise frequently, but in our experience this is usually detected by clinical methods. In our earlier patients frequent X-ray films were taken, until we realized that we were exhibiting an undue amount of radiation which was frequently unnecessary. Chest radiographs are not taken now unless there are special indications, because of physical signs or an unexplained rise of temperature. In all patients chest physiotherapy is carried out by the nurse whenever the patient is turned and by the physiotherapist every four hours.

Feeding presents an immediate problem in almost every case of tetanus. After some early difficulties, arising through pharyngeal ulceration

consequent on the use of an intranasal rubber tube, it became our practice to carry out gastrostomy as one of the first procedures. Later, because vomiting often developed, we tried the effect of jejunostomy, but we soon abandoned this because of the unpredictable effect it had on the absorption of drugs. There are those who condemn gastrostomy on the grounds of its being an unnecessary operation, and if modern polythene tubes have no tendency to produce ulceration this may be true; but in some patients one cannot decide at an early stage whether or not full curarization will be necessary, and without complete paralysis an intranasal tube is likely to be a serious irritant in provoking tetanic spasms. The decision whether to use an intranasal tube or to institute early gastrostomy is therefore still partly unsolved, and so far it has been our usual practice to carry out gastrostomy and tracheostomy at the same time, especially in the young. But whichever method is employed, a balanced diet of not less than 2,500 calories is given together with 2·5 litres of fluid daily. Vomiting is a fairly frequent complication of treatment, especially during the recovery phase, and even though the patient is having chlorpromazine. The dangers of vomiting are obvious, but they are largely overcome by the use of a cuffed tracheostomy tube. Constipation is common to all patients and, as in poliomyelitis, is probably a usual accompaniment of the disease itself. Much more serious is the development of intestinal ileus, for which careful watch has to be kept, the clinical index being the abolition of intestinal sounds. In 2 of our patients ileus became a serious though not a prolonged problem.

Retention of urine is frequent and calls for the use of an indwelling catheter; but under continuous curarization the bladder often empties itself periodically, without distension, and this is especially true of young people. Œdema has been an almost constant feature, and has been seen in patients not totally paralysed. It is usually limited to the eyelids, but it may appear very early and become gross. Occasionally it has been seen in other positions, particularly about the sacrum, but we have reached no definite conclusion as to the cause of this œdema. It always disappears rapidly when paralysis, or other treatment, is stopped.

The use of antibiotics presents considerable difficulty. It is not surprising that these patients are always febrile, because they may well have had both tracheostomy and gastrostomy, not to mention the excision of a wound (which often has to be undergone after admission to hospital), together with very frequent intramuscular injections of drugs. Our early practice was to give intramuscular penicillin throughout but now we use no antibiotics unless there is some very clear indication such as rising temperature or leucocytosis.

It is our practice to carry out frequent laboratory tests. White-cell counts usually show a leucocytosis of moderate severity, but with considerable day-to-day variation. We have, however, seen leucopenia and even agranulocytosis, which in one patient was fatal. Owing to the complexity of treatment, the cause of agranulocytosis may not be certain, but we are satisfied that one causative agent is nitrous oxide, which we now never use and which was probably the major factor in one fatal example. Frequent red-cell counts and hæmoglobin estimations are important because anæmia can develop very quickly, and 7 of our 13 patients required blood transfusion. Daily biochemical assessments are essential during the paralytic regime, because unexplained changes have occurred from time to time and are to be the object of further study. For example, the blood urea is usually raised in the most severe cases. The serum potassium has varied from 3 to 8·5 milliequivalents in the same patient, for no obvious reason. The urinary sodium output is often very low, and this may in part be consequent on sweating, which is often a striking feature, although we nurse these patients completely naked.

With modern methods of treatment nobody dies of tetanus, but deaths resulting from the complications of therapy are still unfortunately frequent. Of our 23 patients 7 have died, 4 while being treated by complete paralysis and 3 while having sedation only; but perhaps we should consider all 7. These included both the youngest and the oldest patients. 1 boy died of asphyxia from a tracheobronchial cast and we felt in retrospect that this could have been avoided by suitable humidification of the air inspired; this complication has not been seen again. An old woman died on the thirteenth day of treatment of bronchopneumonia, and an old man died on the seventeenth day of aspiration pneumonia complicating vomiting. Of those dying during continuous paralysis, 1 boy died of agranulocytosis and septicæmia on the twelfth day of treatment (this was the patient who had been treated for ten days with nitrous oxide). A middle-aged man died of pulmonary infarction complicating a femoral venous thrombosis. A young man died most unfortunately of a sudden and catastrophic hæmorrhage resulting from ulceration of the tracheostomy tube into a major artery—a disaster which we trust will not be repeated. One young woman developed hyperpyrexia, but the precise cause of death was never

established even after autopsy and histological studies. It will be seen therefore that most of the deaths are theoretically avoidable.

Tetanus recovers completely, but we have seen occasional sequelæ. In one of our earlier cases it was found that the respirator was no longer working—though it appeared to be; as a result this patient was subjected to an unknown period of anoxia, and we were not surprised, when his treatment was completed, that he had intellectual deterioration. Fortunately his mental condition recovered completely in the course of a few weeks. We have also seen a precisely similar complication in a patient being treated by positive pressure respiration because of total paralysis from "acute infective polyneuritis"; she too made a complete recovery. 1 man had a prolonged phase of mild pyrexia, the precise basis of which was never established, though he ultimately recovered and returned to work at the coal face. 2 boys have developed contracture of the tendo achillis; 1 of them needed a corrective operation, but histological studies of biopsy material, including electron microscopy, failed to throw any light on the causation of the contracture. We carry out very frequent passive movements of all joints throughout treatment, but whether this will prevent the occasional development of contracture is uncertain. We have seen no other sequelæ.

Finally, it must be remembered that an attack of tetanus confers no immunity on the patient. Therefore it is essential to give active immunization, and the first injection of tetanus toxoid is given before the patient leaves hospital.

The modern treatment of tetanus makes very heavy demands even on the larger hospitals. We have found that the minimal accommodation necessary is a ward normally containing 4 patients. A team of 4 nurses has to be set aside immediately the diagnosis is made, and they may well do no other work but treat this patient for the next month. These nurses carry very considerable responsibility for such things as the giving of drugs and the use of suction. Three consultants see the patient several times a day, two of them being in almost constant touch, and an anæsthetist (of not less than registrar status) is always on immediate call by telephone. Frequent calls have to be made on a variety of specialists. We doubt very much whether any hospital other than a teaching hospital would be able to provide all these facilities. But 13 patients have recovered from severe tetanus and, of the other 10, only 3 were sufficiently mild to survive without elaborate treatment, and we have no hesitation in claiming that the lives of 13 patients, who would not otherwise have survived, have been saved.

Mr. Walpole Lewin (Oxford):

The Management of Prolonged Unconsciousness after Head Injury

The duration of unconsciousness after head injury cannot be foretold at the outset with any accuracy. The essential aims of treatment, which will be outlined briefly in this communication, are therefore applicable to all major head injuries. It is not proposed to discuss the causes of prolonged unconsciousness, or the place of surgery in the group associated with cerebral compression from intracranial hæmatoma or œdema, but to concentrate on those medical and nursing problems associated with the unconscious state. By prolonged unconsciousness is meant a state where the patient remains in coma, or sufficiently unconscious to be unresponsive to speech and unable to swallow requiring artificial feeding, for a month or more. In practice this period divides the many patients who are unconscious for a week or so, and in whom recovery can be expected for the majority, from those patients with longer periods of unconsciousness and more serious implications. The prognosis in patients unconscious for long periods is difficult and in this paper the results of treatment of 102 patients unconscious after head injury for more than one month at the Radcliffe Infirmary, Oxford, and the Military Hospital (Head Injuries), Wheatley, Oxon, are summarized.

Essential Treatment

The basic aims of treatment should be a free airway for twenty-four hours a day, maintenance of the blood pressure, control of the patient's temperature and a satisfactory nutritional state. The prevention and treatment of chest complications and the use of tracheostomy in these patients have been dealt with elsewhere (Lewin, 1959).

If the blood pressure is allowed to fall then cerebral ischæmia may follow and its effects added to the existing brain damage. In one patient, for example, with head and limb injuries, a period of hypotension secondary to blood loss from a fractured leg was accompanied by the sudden onset of a left hemiplegia. At times the poor colour of a patient may be due more to a low blood pressure than an imperfect airway. Early and adequate blood transfusion where indicated or fluid replacement in others can transform not only the general condition but may lead to improvement in the level of unconsciousness and in the neurological disability. As a short-term measure in some patients we have found the phenylethylamine derivatives (Methedrine) useful, but our experience with noradrenaline in unconscious patients with a falling blood pressure from head injury or brain-stem vascular lesions has

been usually disappointing. Following the recent observations of Burn and Rand (1959), it may be that a better result will be achieved in the future by restoring the blood pressure initially with noradrenaline and maintaining it with Methedrine.

It is also necessary to control the temperature in these patients and in the early days hyperthermia is a common, and can be a fatal, complication. An attempt should be made to keep these patients normothermic. In most instances simple measures suffice. The patient should be nursed in a cool room and covered by a single sheet. If the rectal temperature exceeds 100° F. (38° C.), tepid or ice sponging should begin, and if the temperature does not respond an ice-water enema administered. These measures should begin early, since if the temperature is allowed to climb above 102° F. (39° C.) it may not be reversible. Alcohol sponging and 1–2 grammes aspirin *per rectum* have also been advocated. If these measures are not adequate then chlorpromazine intramuscularly and the application of ice bags to the body surface are indicated. This essential need to control the temperature should be sharply differentiated from the particular treatment by hypothermia (*see below*).

From the outset these patients require an adequate amount of fluid, and after the first few days protein feeding should begin to offset the rapid protein catabolism with wasting which develops. Although a limited period of moderate dehydration may be advised for selected patients with raised intracranial pressure, routine limitation of fluid does more harm than good. We feed these patients through a small polythene or rubber gastric tube and aim at an average intake of 5 pints in 24 hours of milk and water with added glucose. Later a higher protein diet containing 100 grams protein with a caloric content of 2,200 is given, and in the third stage a 2,700 caloric diet with 130 grams protein.

Special Methods of Treatment

(1) *Hypothermia.*—The advance of anæsthesia in the last ten years has stimulated further interest into the possibilities of hypothermia. A limiting factor in the surgery of the great vessels and of cerebral aneurysm is the sensitivity of the brain to anoxia. It has been shown in dogs that as the temperature falls so does the oxygen requirement of the brain so that at 30° C. the need is reduced by 55% (Rosomoff, 1956). Rosomoff also showed that ligation of the middle cerebral artery in dogs at 25° C. did not lead to massive infarction. One of the main uses of hypothermia in neurosurgery at the present time is in the surgery of subarachnoid hæmorrhage. Laborit and Hugenard (1951) used hypothermia in some cases of severe head injury. There are several theoretical advantages. During the dangerous early days of unconsciousness after head injury, hypothermia may minimize the added effects of hypoxia produced by cerebral œdema or secondary to respiratory difficulty, and thereby protect uninjured brain or damaged but recoverable brain. It is also known that as the temperature falls so does the intracranial pressure. Other beneficial side-effects which may be observed are that as the temperature falls hyperpnœa and bronchial secretion lessen with consequent improvement in the airway; spasticity of the limbs passes off; and the risks of some metabolic disorders such as dehydration and alkalosis diminish.

On the other hand the observations of Knocker (1955) on systemic tissue injury under hypothermia and their similarity to the reaction to stress has to be remembered. Other complications of hypothermia, especially ventricular fibrillation, have also been described. These problems, however, are mainly associated with temperatures below 90° F. (32·2° C.) whereas the beneficial effects as they might influence head injury have been seen at higher and safer levels.

In the last four years we have selected 39 patients in coma from head injury for this treatment. The temperature has been maintained at a level of 90° to 95° F. (32·2–35° C.) for a period of five to six days using chlorpromazine and promethazine together with the surface application of ice bags (Lewin, 1957). 22 of the 39 severely injured patients survived. Patients with added cerebral compression from intracranial clot or from severe contusion or laceration did badly and the quality of recovery in the survivors has not suggested so far that much has been gained by hypothermia in this group. On the other hand, of 17 patients with prolonged unconsciousness but without a severe compressing agent other than cerebral œdema, 11 survived and with one exception have gone on to make good practical recoveries. This is encouraging and at present we feel that hypothermia may have a place in the treatment of the patient who remains unconscious with decerebration, hyperpnœa and pyrexia from a diffuse cerebral injury.

(2) *Hypertonic fluids.*—Operation may be needed for some cases of cerebral compression. Medical measures to combat raised intracranial pressure from cerebral œdema have been practised for a long time. It has already been stressed that routine dehydration of the unconscious patient can do more harm than good but moderate dehydration for a limited period by restricting the fluid intake to 3 pints a day and administering a saturated magnesium sulphate enema, 6 oz. twice daily, can be valuable in the

early days when the intracranial pressure is known to be high. Where a more rapid response is needed, 50% sucrose intravenously has been used for many years but its subsequent reaction with a further rise of intracranial pressure has led to the trial of other substances. Hypertonic plasma, triple or quadruple strength (Hughes *et al.*, 1938; Turner, 1941), seems to be a satisfactory alternative, given rapidly in amounts of 100–200 c.c. Javid (1958) has recently reported favourably on the use of urea intravenously in lowering intracranial pressure following a suggestion of Fremont-Smith and Forbes (1927).

(3) *Drug therapy.*—Acetylcholine is released into the C.S.F. after injury and, based on this, Ward (1950) reported favourably the use of atropine up to 1/10 grain subcutaneously for unconsciousness after head injury. In 1950 we treated a few patients with this method choosing those in whom further help was required, that is this group with prolonged unconsciousness of a month or more. Doses of up to 1/10 grain subcutaneously were injected and atropine was also injected into the cerebral ventricles in doses up to 1/150 grain. In these cases we saw no beneficial effects on the conscious level and the only changes seen were the peripheral effects of drying up of the bronchial secretions, temporary lessening of spasticity, and dilatation of the pupils. Hughes (1957) could find no correlation between the amount of acetylcholine in the C.S.F. and the depth of unconsciousness.

The use of *chlorpromazine* has already been mentioned in connexion with hypothermia. It can, however, relieve muscle spasm and diminish tonic fits, and is also thought to have an anti-œdematous action and inhibit the reaction of the reticular substance. It can be used therefore on its own or in conjunction with promethazine and pethidine to control hyperpnœa and spasticity but we have not seen improvement as such in the unconscious state.

Complications

Metabolic Disorders.—Biochemical studies on a consecutive series of 76 patients unconscious after head injury revealed the frequency of metabolic disorders (Higgins *et al.*, 1954). Some are transient but others are serious. By comparison with their occurrence in other conditions there is no doubt they play an important part in the mortality of head injury. Their prevention and treatment are therefore important. Regular biochemical examination of the blood and urine is invaluable but simple ward tests can do much to recognize these problems early. A fluid balance chart should be kept and the urine examined daily for sugar and albumin, the chloride excretion measured by the Fantus test (an unreliable but rough guide) and the specific gravity taken. These tests, with periodic estimations of the blood urea, can indicate the need for a more formal biochemical study if abnormalities are found.

Water deprivation and *alkalosis* should be infrequent as the basic treatment of the unconscious state is better understood but disorders of *sodium and chloride balance* and *renal uræmia* remain major hazards. Inability to excrete the chloride ion with hyperchloræmia usually develops in the early days of the unconscious state and has been seen in all age groups. If recognized early it can be reversed by omitting sodium chloride from the diet and increasing the fluid intake. On the other hand excessive loss of sodium and chloride ion in the urine with the accompanying features of dehydration arises in the later weeks and usually in older patients. So far attempts to reverse this process by Eucortone, deoxycortone acetate and cortisone have failed but the condition, which may be protracted and unpredictable, can often be held in check by increasing the fluid intake and a high salt diet. When unrecognized, the condition leads to rapid wasting and decubitus ulceration.

Acute renal failure with tubular necrosis can follow severe head injury. In some instances the presence of multiple injuries, a history of previous renal disease or a phase of hypotension raises possibilities of several ætiological factors. But in other cases the evidence for a central cause is substantial. In a recent case of spontaneous intracranial hæmorrhage in a boy aged 15, for example, where there were no other extraneous factors involved, renal failure developed within twenty-four hours with death on the eighth day. Hoff *et al.* (1951) and Cort (1953) have demonstrated experimentally by electrical stimulation of the brain a relationship between brain and kidney.

The possibility of renal failure, therefore, has to be borne in mind in the management of the unconscious state. Treatment to be effective has to begin early. Taylor (1957) from a study of these patients suggested that from a therapeutic point of view, patients who showed a blood urea level higher than 100 mg.% together with urine urea levels below 2 grams% should be considered as having a degree of renal failure and corrective treatment should begin. The simplest treatment consists of restricting the fluid intake to balance loss and the provision of a high-calorie, non-protein diet by the administration of 10% or 20% glucose solution by the gastric tube. In some of our earlier cases we used a polythene catheter into the inferior vena cava but were discouraged by the risks of thrombosis. Shaw (1959), however, has reported greater success with this method. If the kidney function does not improve under these

regimes, then the future clearly lies with the artificial kidney which undoubtedly will be used more in the future.

Another important metabolic disorder to consider if unconsciousness is prolonged is the *change of weight*. In the early weeks these patients waste rapidly in spite of high protein diets, and unless care is taken, decubitus ulcers and progressive emaciation may develop. In addition to diet, repeated small blood transfusions have been found invaluable during this period. The androgens also have a place. Testosterone was used in the earlier cases but more recently we have found norethandrolone (Nilevar) very helpful in promoting protein anabolism. It is important to recognize, however, that this weight loss is normally limited to the early weeks. After six weeks, and particularly in younger patients, there is a tendency to obesity. A patient may gain several stones and this disadvantage in the setting of a paraparesis or hemiparesis is of course obvious. High-protein feeding, therefore, can be overdone and once the weight of the patient has returned to normal it should be maintained at that level by dietary means. Fortunately the gain of weight in many instances seems to be self-limiting and some of these patients who have been seen some years after the injury have lost much of their obesity.

Gastro-intestinal Complications.—Gastric and œsophageal lesions have been described for many years in association with intracranial diseases with unconsciousness. Œsophageal rupture, gastric and intestinal erosions with and without hæmorrhage have all occurred. These complications are often terminal and there is little that can be done to prevent them. However, the possibility of treatment in isolated cases should be borne in mind. Fincher and Swanson (1949) described a successful case of suture of œsophageal rupture, the physical signs of which have been described by Maciver *et al.* (1956). In one of our cases a partial gastrectomy was successfully performed for severe bleeding from a gastric ulcer. In another case massive blood transfusion failed to save a patient unconscious one month after head injury who developed severe rectal bleeding. Autopsy showed a hæmorrhagic mucosa only.

Spasticity and Contractures.—One of the most important and most difficult items in the management of prolonged unconsciousness is the relief of spasm and the prevention of deformity. Physiotherapy is required for these patients from the outset, not only on behalf of the chest but for the limbs, and as a general rule they should be turned two-hourly night and day. Spasticity in the early stages can be helped by cooling the patient and the use of drugs as already indicated but these methods are of little use later on. Phenobarbitone, Benadryl and Myanesin all help the mild case from time to time but have no worth-while effect in the severe continuing spastic state. In addition to moving the limbs gently through their range every day, the most useful measure to prevent flexion deformity is to nurse the patient on his face. This is always possible after the early days are over even with a tracheostomy, and we now look on this posture as an essential feature of treatment. Ultimately these patients spend several hours by day and night lying prone. The weight of the limbs and the stimulus of the extensor thrust in this position does more than any manipulative physiotherapy to minimize contracture. In some later cases weights may be suspended from the heels for short periods only but our experience with corrective plasters or more formal traction in frames has been uniformly disappointing and carries considerable risks of skin ulceration. A further useful measure is to get these patients out of bed as soon as it is practicable. A chair can be adapted to support them and even attempts to stand these patients supported on each side all help to develop the extensor thrust and prevent contractures.

Heterotopic Ossification.—Calcification and ossification in the soft tissues in association with various neurological conditions such as tabes dorsalis, syringomyelia, poliomyelitis and paraplegia is well known. Our attention was drawn to a similar occurrence in some cases of prolonged unconsciousness after head injury when seeking for an explanation of why some patients developed increasing stiffness of certain joints, particularly the shoulder, elbow, hip and knee. It may remain mild and self-limiting but at times can be severe and progressive. Its recognition is important since vigorous physiotherapy in an attempt to overcome the stiffness can only make matters worse. Our practice, therefore, is to X-ray suspicious joints from time to time if it is thought that this complication is a possibility.

Results

Although the outlook for a patient is always serious as long as he remains unconscious, it is also true that some patients can survive long periods of unconsciousness and make practical recoveries. As a general guide the results in our series of 102 patients, who have remained unconscious after head injury for periods of one to sixteen months, may be mentioned briefly. 63 survived and 39 ultimately died. Of the 63 survivors, 19 recovered sufficiently to return to their former work and scholastic level. To take

two examples, one patient went on to take G.C.E. in seven subjects successfully and another patient successfully managed a university teaching course with commendation. A further 29 patients made practical recoveries so that they were back at work or working in their homes, although with some mental or physical disablement compared with their pre-accident status. A practical recovery took place therefore in 76% of the survivors. 15 patients were left severely disabled and although 9 of them returned home and some to work in sheltered workshops, the price of survival was a heavy one.

If a good recovery is to be made, then some improvement is to be expected within one month of injury. This is not to say that consciousness will have been regained, but at least there should be more response to pain, the spasticity beginning to pass off and the limbs moving purposefully at times, and the pupils reacting to light. The longer the period of coma the worse the prognosis. During this period of unconsciousness, degeneration in the nervous pathways secondary to the injury is going on and serial air studies can be valuable in assessing the degree of change and in the light of experience the likelihood of a practical recovery. We have not seen a patient recover who has shown a gross and progressive ventricular dilatation as the weeks go by.

A final word should concern the families of patients who are unconscious for long periods. The situation can be a difficult one to sustain. It is important to see the relatives at regular intervals and to encourage them gradually to take up their normal lives again so that a whole family is not needlessly disrupted whilst the patient remains many weeks in hospital unconscious. Should the patient recover he will need a good deal of help at home for many months to come and it is essential that he returns to an integrated and above all a rested family and one not worn out by months of vigil.

It is clear that the management of prolonged unconsciousness is no longer a matter of waiting to see what the outcome will be. There is a good deal of active treatment to plan during the acute and later phases, both preventive and corrective; and expert nursing needs to be continued for many weeks. There are naturally many disappointments but it is important to remember that a number of these patients can survive and make practical recoveries.

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Meeting
March 20, 1959

Argininosuccinic Aciduria. A New Form of Mental Deficiency Due to Metabolic Causes

By C. E. DENT, M.D.

London

IN the *Lancet* of last year we described our preliminary investigations on two severely mentally retarded sibs who came from a large family all otherwise normal (Allan *et al.*, 1958). They both showed a very gross abnormality of urinary amino-acid excretion, namely a large output of an amino acid readily detectable by paper chromatography, but which did not behave as any known amino acid, and which we were unable to identify. Further clinical features were that one of the sibs had had epileptiform attacks, both had grossly abnormal EEGs and both possessed friable hair which broke off readily after a short period of growth. Otherwise their general health was excellent. The unknown metabolite was present in larger quantity in the cerebrospinal fluid than in the plasma, and had a high renal clearance. We speculated that it was probably formed in the brain owing to some inborn error of metabolism. The unknown amino acid was clearly rather complex since it readily decomposed into other substances, also unidentified. We thought it might have been a peptide resistant to acid hydrolysis since very prolonged hydrolysis led to the liberation of small quantities of aspartic acid and of ornithine.

Further work from this Department, briefly reported elsewhere (Westall, 1958; a fuller paper is being prepared) has now enabled a definite identification of the unknown to be made. It is argininosuccinic acid (Fig. 1), a substance that has recently been shown to play a most important part as an intermediary in the ornithine cycle of urea formation. It is a considerable problem to us in our interpretation of the disease process to note that both affected sibs had normal plasma ureas and urine urea outputs in spite of what would at first sight be considered as a metabolic block in the formation of urea. Bearing in mind, however, that our previous work suggested that the compound was formed by the brain, it would seem more likely that the metabolic block concerned some hitherto unknown synthetic process in brain metabolism, and that the disease has kindly presented us with the opportunity for discovering and studying this. The two sibs each excrete about 3 grams a day of argininosuccinic acid in their urine. Further preliminary metabolic investigations have been carried out and are being continued. We now suggest that the disease should be named as in the title of this paper.

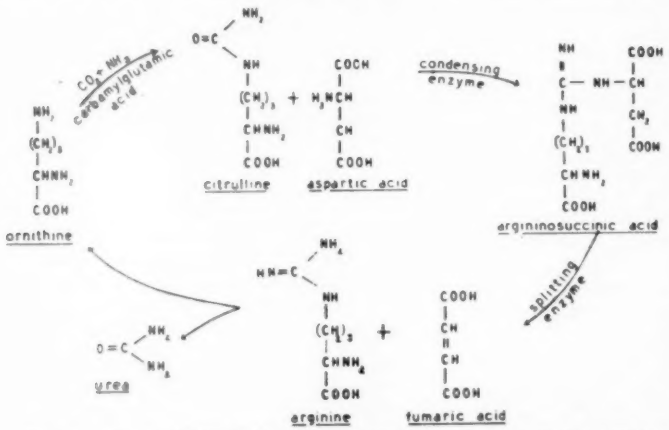

FIG. 1.—The ornithine cycle. Reproduced from Ratner (1954) by kind permission (copyright by Interscience Publishers, Inc., New York).

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Anorectal Agenesis with Persistence of Cloaca

By M. H. Gough, F.R.C.S.

London

The term cloaca conjures up memories of embryological studies or ideas of gross irremediable congenital deformities in the newborn. The latter, as I hope to show, is far from the truth; the embryological memories will have to be supplemented by a brief reiteration of the development of the hind end of the embryo.

The development of the tail fold leads both to the formation of the hind-gut and the cavity which receives the hind-gut, the developing mesonephric ducts and the allantois; in other words the cloaca. Embryologically the term cloaca refers to the cavity receiving alimentary, urinary and genital ducts. This is also sometimes called the endodermal cloaca for its epithelium is derived from that germinal layer, as opposed to the so-called ectodermal cloaca which develops as a depression on the ventral or ectodermal aspect of the cloacal membrane. Clinically one maintains the same criteria of definition, but the cavity itself does not necessarily represent exactly the same cavity as the embryological cloaca. It is, in fact, usually only a small part of it. It is important to stress this difference between the embryological definition of the term cloaca and the sense in which it is to be used as a clinical description. There is considerable variation of opinion regarding the nomenclature of congenital anorectal deformities, and the term cloaca has been used to describe more than one type of abnormality, as will be mentioned later.

To revert to the embryology, the cloaca now becomes divided by the growth, in the angle between the allantois and the hind-gut, of the urorectal septum: this extends caudally to divide the primitive rectum from the primitive urogenital sinus. The remaining small communication between the rectum and urogenital sinus, before the septum reaches and fuses with the cloacal membrane, is called the cloacal duct. The primitive urogenital sinus thus formed may be divided into the vesico-urethral segment above the openings of the mesonephric ducts, and the definitive urogenital sinus below these openings. The former is destined to become the bladder and posterior urethra, and the latter, according to sex, most of the distal urethra in the male or the vestibule in the female. The mesonephric ducts form the vasa in the male and virtually disappear in the female. At this time also, the tail gut—the most caudal part of the cloaca—regresses and disappears. The cloacal membrane then breaks down so that free communication exists between the ectodermal and endodermal cloaca.

The remaining aspect of embryology relevant to this discussion is the formation of the female genital tract. The müllerian ducts develop from the cœlomic epithelium just lateral to the mesonephric ducts, and caudally they cross in front of the mesonephric ducts and grow to meet and fuse with their fellow of the opposite side to form the uterovaginal canal. The caudal end of this canal meets the posterior wall of the urogenital sinus and produces there an elevation—the müllerian tubercle. Proliferation of cells from the region of the müllerian tubercle results in the growth of a solid cord of cells, the vaginal cord, which increases the distance between the uterovaginal lumen and the urogenital sinus. There is still some controversy about the origin of the lower vagina, the generally held view being that it is formed entirely by the recanalization of the vaginal cord. However, Koff (1933) postulates that the lower vagina is formed from the sino-vaginal bulbs which develop from the urogenital sinus, and McKelvey and Baxter (1935) pointed out that abnormalities found supported the view that the vagina was of composite origin. This is borne out by examination of some of the cases under discussion. The question of the origin of the vagina also affects that of the origin of the hymen. If the whole of the vagina develops from the vaginal cord, then the hymen represents the remains of the cloacal membrane; if partly from the sino-vaginal bulbs it represents the junction between these bulbs and the vaginal cord.

In describing anorectal abnormalities we meet the difficulties in nomenclature which I mentioned. Swenson (1958) groups all these abnormalities under the heading "imperforate anus". This is perhaps not wholly suitable although the word anus may be used in its purely embryological sense as the termination of the bowel, or in its usual clinical sense as the termination of the bowel complete with sphincter mechanism. I propose to call these cases rectal or anal agenesis with fistula formation, as appropriate. Nixon (1959) has classified the case of high rectal agenesis with rectovaginal, rectovesical or rectourethral fistula formation as a cloaca, using as a synonym "imperforate rectum". This nomenclature has advantages in that, used in conjunction with the terms vulval ectopic and perineal ectopic anus (Browne, 1955) it serves to divide these lesser abnormalities from the more serious ones where the bowel terminates *above* the pelvic floor. In the former, some form of minor surgery such as a perineal cutback will be

adequate for treatment, whilst in the latter some form of major surgery will be needed. This conception of a "cloaca" is not new and has been used by several writers in the past, including Pennock and Stark (1926) and Stone (1936).

The following cases may show that the term cloaca should be reserved for more serious abnormalities occurring from some arrest in development at a fairly early stage. One congenital abnormality may be accompanied by another, and the occurrence of an earlier fault in the embryo might be expected to be more frequently associated with other, often severe, abnormalities which may radically alter any plan of treatment. This is, in fact, what is found to occur.

The following examples of what I term cloaca have been collected from the records of children treated at the Hospital for Sick Children, Great Ormond Street, over the past ten years. A few of these seem to be little more than examples of the more usual anorectal anomalies with a somewhat abnormally situated urethra: in the examples a gradual regression towards the primitive form may be seen, some of them approximating to the normal conditions found in marsupials, amphibians and reptiles, as one descends the evolutionary scale.

FIG. 1.

One example of a typical cloaca is diagrammatically represented in Fig. 1. This girl had a laparotomy, division of what I must call the rectocloacal fistula and a pull-through of the rectum. She is well apart from considerable residual trouble with colonic inertia, and it is interesting to note that she is fully continent of urine. By no means all of these children have a urinary sphincter, as is seen in Fig. 2 which shows a considerably more primitive state of affairs. Here there was a vesicocloacal orifice which

FIG. 2.

accepted two fingers and a rectocloacal orifice which accepted one finger. Neither orifice had any evidence of a sphincter and there was absence of the uterus and both fallopian tubes, although both ovaries were present. This girl had a defunctioning colostomy, isolation of the distal sigmoid loop and, later, a bilateral ureteric transplant into this isolated loop. She is alive and well in spite of the obvious disadvantages of a colostomy and a urinary diversion.

Further abnormalities may complicate the picture and Figs. 3–6 illustrate four such examples:

Fig. 3 shows two commonly associated anomalies, a double uterus and also a mucocolpos. The former occurs in the majority of the 18 cases of cloaca I have collected and is, in itself, of little importance with regard to treatment. The mucocolpos may be very large and may present as an abdominal tumour. It may be mistaken

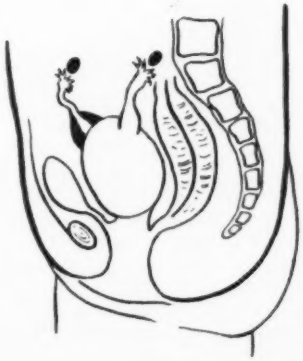

FIG. 3.

for an enlarged bladder and it will be difficult to disprove this because of the abnormal position of the urethra. An awareness of the occurrence of mucocolpos will be sufficient to prevent its inadvertent removal, along with a compressed and adherent bifid uterus, tubes and ovaries, as a dermoid or retroperitoneal cyst. This child died of peritonitis and septicæmia following drainage of the mucocolpos—which turned out to have been infected—and pull-through of the rectum (which incidentally was duplicated, this being found at autopsy).

Fig. 4.—This girl again had a double uterus, but the main point of interest is the presence of one

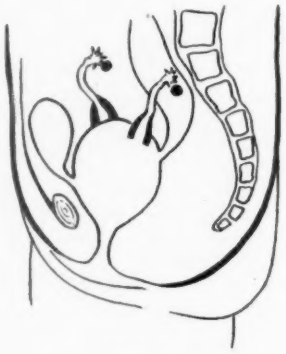

FIG. 4.

small external orifice which was taken at initial examination to be the external urinary meatus. At operation perineal dissection was performed and a pull-through completed of what appeared to be the rectum. Post-operatively she developed intestinal obstruction and laparotomy revealed that what had been pulled through was the cloaca itself, and following this the rectocloacal orifice had become obstructed. A transverse colostomy was then performed and she made a good recovery. She was readmitted at the age of 1 year for pull-through. This was successfully carried out, but she unfortunately died of gas gangrene following later closure of the colostomy.

Fig. 5. again shows a more primitive form. Here there is a double uterus and vagina, the bowel opens into the cloaca via the septum between the two halves of the vagina, and the bladder opens widely and directly into the anterior cloaca. There is a cystic reduplication of the terminal bowel, which alone represents large bowel. This child died in a cyanotic attack two days post-operatively. She had gross renal abnormalities and probably congenital heart disease also.

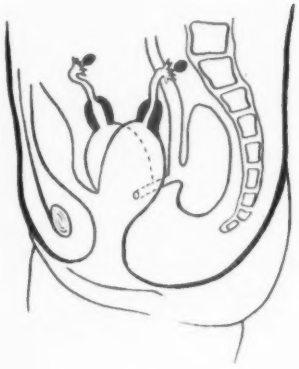

FIG. 5.

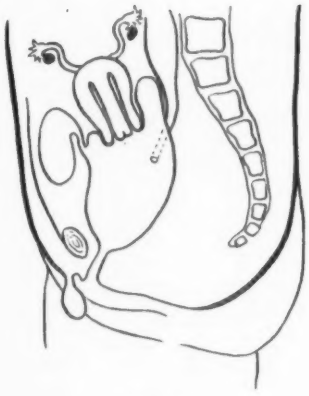

FIG. 6.

Fig. 6.—This child has a cloaca with an apparent pseudohermaphroditism.

An easily recognizable deformity seen in 2 cases has been the presence of a tube-like fold of skin representing the phallus. Birnbaum (1912) referred to the fact that complete absence of the genitalia occurs only in conjunction with severe abnormalities such as cloacal formation or sireniform monsters. I have not seen any reference to this tube-like phallus, but its presence should suggest the presence of a cloaca. In one child it overlay a single orifice, and in the other it provided an outlet for the cloacal orifice.

All the examples of true cloaca which I have shown are females; in these children the existence of the genital cavity makes the decision as to

whether or not a cloaca is present more easy. Whether anorectal agenesis with recto-urethral or rectovesical fistula in a male should be termed a cloaca is, from the practical point of view, unimportant. This problem, strictly speaking, rests on the site of the uterus masculinus and openings of the vasa.

Several points arise from these 18 cases—six, or one-third, are alive; 11 have died; and one I cannot trace. I have arbitrarily divided the deaths into those which were probably inevitable due to other serious abnormalities and those which were possibly avoidable taking our present surgical armamentarium into account.

Of the 11 deaths, 6 were probably inevitable and 5 might have lived apart from the onset of some form of sepsis. 5 children died in cyanotic attacks in cardiac failure or bronchopneumonia, 4 died of septicæmia, peritonitis or gastroenteritis, and 2 died directly of gross renal anomalies.

The associated abnormalities most frequently found were: (1) Œsophageal atresia, (2) upper renal tract abnormalities, (3) congenital heart disease and vascular anomalies, (4) anomalies of vertebral, especially sacral, development. It is probably always worth while passing a nasogastric tube on these infants; in 1 of these 18 an œsophageal atresia was missed until after the operation for the cloaca. Should the infant survive it is wise to perform an intravenous pyelogram to exclude upper renal tract abnormalities which may require attention, although in the absence of urinary infection this investigation is probably better done, from the point of view of good pictures and decreasing the radiation risk, at about 1 year of age. The incidence of such abnormalities in straightforward cases of anorectal agenesis is surprisingly high. It is even higher in these more unusual children.

The first aim of management is to discover, as far as possible, exactly what the anatomy is. From this series an associated abdominal tumour is more likely to be a mucocolpos than an enlarged bladder. The usual X-rays to show the level of the rectal gas bubble will help and, in addition, will show any bony deformity of the sacrum. An examination under anæsthesia of a single orifice or cavity may help, although the presence of meconium and mucus may make interpretation difficult. It may be possible to catheterize the abnormally placed urethral orifice and perform cystography. A mucocolpos should be drained. Whether an immediate abdominoperineal operation for rectal pull-through should be performed depends on individual circumstances: in the absence of other abnormalities this is the ideal treatment.

In some children, such as my second example, there can be no chance of urinary continence; in others it will have to be left to time to establish whether control exists. The possibility that an operation for urinary diversion on to the abdominal wall may be needed at some later time should be borne in mind. One of the serious complications of the abdominoperineal pull-through operation is damage to the pelvic splanchnic nerve plexuses supplying the bladder and its sphincters. These plexuses lie lateral to the normal rectum and probably lie close to each other in the mid-line in cases of anorectal agenesis. They are, therefore, especially at risk during the perineal dissection in the male; in the female the presence of the mid-line vagina may protect them. Whilst the actual operation is easier in the neonate, due to the relative shallowness of the pelvis, it may be that further deforming abnormalities such as a mucocolpos should be reason for performing an initial transverse colostomy.

It may be much easier to plan a surgical approach to the problem of urinary incontinence and anorectal agenesis when the child is a little older. Should continence exist it may be easier to visualize and avoid the important splanchnic nerves. Whenever laparotomy is performed a full note should be made of the state of the internal genitalia. Questions by the patient in later years regarding getting married and having children will be difficult to answer unless operation notes are complete.

I hope I have been able to show that the condition of persistence of the cloaca is not such a hopeless one as might be thought. Reports in the literature are few; it is possible that in the past some of these cases were classified as "fœtal ascites"; I have certainly found one such in the literature of fifty years ago. With the aids to surgery available to-day there seems no reason why the lives of the majority of these children should not be saved.

Acknowledgments.—I would like to thank the surgeons at Great Ormond Street for permission to refer to cases admitted under their care, and especially Mr. D. Innes Williams who first drew my attention to this interesting condition.

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"Sudden and Unexpected" Death in Infancy [*Abridged*]

By JOHN L. EMERY, M.D.

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WITH the great diminution in child death a major problem in diseases of children is that of death occurring either unexpectedly or following a very brief illness in what appeared to be a normal healthy child. Contrary to other diseases such as mental, physical and metabolic defects, these children, but for this peculiar accident of disease, would apparently have lived a completely normal life.

The problems involved are wide. Four points are discussed here: (1) The meaning of "acute disease, sudden or unexpected death". (2) The magnitude and the general pattern of disease found. (3) The general epidemiological approach to these deaths, and (4) Some clinical case histories with a view to stimulating interest in this aspect of the problem.

First, what is meant by "sudden and unexpected death"? Emery and Crowley (1956) made a careful study of case histories of a consecutive series of 50 children reported to the Coroner as "Sudden, unexpected death", and found that over half had shown symptoms of some disorder for more than forty-eight hours prior to death. Is it a matter of accident as to whether a child dies "suddenly" at home or is sent into hospital and dies there? Does this account for the discrepancy in the proportion of "sudden" deaths of children in different areas (Banks, 1958; *Lancet*, 1958)?

To assess the magnitude of the problem we have studied all children dying with recorded symptoms of less than forty-eight hours' duration. Our figures for the relative incidence of children dying over the age of 7 days with a history of symptoms less than forty-eight hours are shown in Fig. 1; the proportion of deaths remains almost stationary. There are fallacies in these figures: during the past ten years there has been a diminution in the number of child deaths in this age group and yet within the hospital we have had no diminution. This is due to the increasing numbers of children that are being referred to the hospital from outside areas. The "sudden and rapid" deaths do not come from great distances. During recent years, I have spent a great deal of time taking histories from relatives of children who died apparently suddenly, and this has meant that a number of children who previously would have been classified as sudden deaths now have to be taken out of this group. It will be seen that the total number of children dying from acute illness has remained virtually stationary and constitutes in our hands approximately 40% of deaths. If one were able to eliminate the errors in a satisfactory way, it is probable that acute illness would constitute approximately 50% of deaths. The Registrar-General (1955) showed that over 20% of deaths between the ages of 2 weeks and 2 years were certified to the Coroner, and Banks (1958) found that sudden death formed 44% of deaths in that age group in the Cambridge area. The differences in the proportions of children reported this way depend in our opinion largely upon the amount of care taken in the history taking.

Since the comfortable mythology of status thymolymphaticus has been given up, morbid anatomists can find no convenient pigeonhole for these deaths. We find, in company with most observers (Bowden and French, 1951; Barrett, 1954), a wide spectrum of recognizable disease in these children, but a core of children in whom no anatomical lesion at all is found.

In a series of 1,250 necropsies in Sheffield, 654 died over the age of 7 days, and of these 267 (40%) died with symptoms of less than forty-eight hours' duration. 125 died at home, 13 in the ambulance, and 129 in hospital. 10 died as the result of an unnatural accident, 8 the late result of a "cold" operation in hospital, leaving 249 apparently natural deaths. Of these, 83 showed disease of long standing of which approximately half had been suspected during life. In 145 some lesion was found at necropsy and in 21 no lesion, but few would of themselves have been adequate to cause death. The age pattern of these diseases shows that certain diseases such as polio-encephalitis and Waterhouse–Friderichsen syndrome appear to occur at definite ages, but

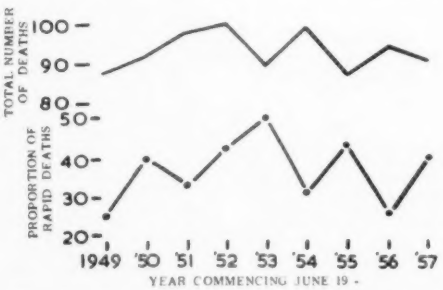

FIG. 1.—Showing the proportion (percentage) of deaths due to disease of less than forty-eight hours' duration in children coming to necropsy through the Sheffield Children's Hospital, during the period June 1949–July 1958. Children over the age of 7 days.

that the "no cause of death found" group, together with that of infections of the respiratory tract, is centred in the age group 1 to 5 months.

From a general epidemiological viewpoint a study of the sites of death related to day of week (Emery, 1959) suggests that almost as many children die of acute disease during the week as at weekends, but death is more likely to be at home at the weekend and in hospital during the week.

This has led us to examine the environmental aspects of these deaths.

Case Histories

Case I.—Carol was the 6-weeks-old second child of a family living in a relatively isolated house with one guest. She had shown no signs of respiratory infection since she had been born in hospital. On the Sunday of the first week in February, the father came home from work with "flu" and catarrh and was at home all that week. On the Friday evening, baby Carol was put to bed, not having taken a complete feed. The sibling, Paul, showed no symptoms, but that night, for the first time for months, he was restless and awoke several times. The child Carol was found dead in bed on the Saturday morning. On the following Monday, both the mother and the guest of the house went down with "flu".

Case II.—Roy was the only child of young parents, again living in an isolated house. He had had no signs of any infection or disease after birth, and was now aged 4 months. On Monday he was taken by his mother to an Infant Welfare Clinic for the purpose of having a triple injection. There the mother and child were placed in a room with other children, many of whom had colds. Three days later Roy vomited. Later in the day he had loose stools, and he died unexpectedly during the night. A streaming cold commenced in the mother the following evening and the cold appeared in the father four days later.

In both these cases we have apparently a first infection in a child, the child succumbing apparently in the invasive phase of the "cold".

Cases III and IV.—These children, Kelvin and Charles, died in a village in the West Riding close to Sheffield; they were cousins, in two separate houses, the mothers of the children being sisters.

Kelvin, aged 2 years, commenced a respiratory tract infection, and was ill for two to three days. He was then thought to be better. His aunt, the mother of Charles, was frequently visiting the house, and when Kelvin died unexpectedly five days later she stayed with her bereaved sister. Thus on the night of the next day, Charles' father was looking after him, and put him to bed. Charles apparently had had no signs of infection since birth, and was now 2½ months old. He had not taken all his feed, and was a little restless on going to bed. His father found him dead in bed the next morning. Kelvin died with pneumonia, from which we grew *Staphylococcus aureus*, and Charles died with acute bronchiolitis, also due to *Staphylococcus aureus*.

Case V.—David was one of a small family living in a block of four houses joined by a yard. In the chart shown (Fig. 2) the occupants of these houses A, B, C, and D, were as follows. In A, the family in which the child died, were the mother, father, Carol aged 9 years, Sandra aged 3 years, and baby David. The second house, B, contained an old gentleman who lived alone. House C contained an elderly woman and her grandchild Susan aged 3 years, who came to stay because of illness in Susan's home. In the far

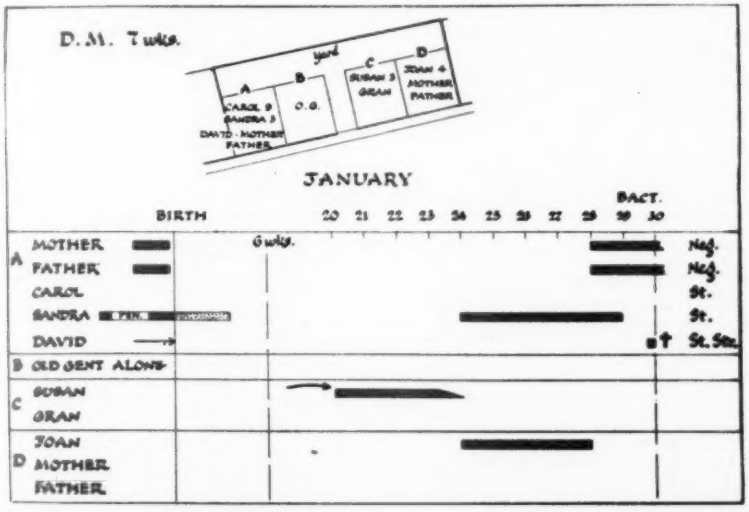

FIG. 2.—Diagram of the layout of the group of four houses, A, B, C, and D, around a yard, and the course of an infection throughout the small community and the death of baby David.

house, D, was a family consisting of mother and father and a girl Joan aged 4 years.

Apparently Susan's cold started on January 20, the day after she arrived at house C. Four days later Joan and Sandra commenced with a cold. Four days after that both the mother and father of Sandra commenced colds. The mother did all the nursing of baby David with a mask. Baby David was found dead in bed on January 30, having had no definite symptoms.

We isolated beta-hæmolytic streptococci and *Staphylococcus aureus* from David, Sandra and Carol. The staphylococcus from David and Carol was of the same phage type, that from Sandra was different. The previous history from this family was that David's birth followed after a cold in both father and mother and Sandra, for which Sandra had been treated with penicillin. The mother's and father's colds had disappeared at the birth of the child; no cold had gone through the house for the six weeks prior to this epidemic.

Here we see an infection running through a family apparently striking the baby during the latter part of the incubation period.

This type of history is not confined to "flu", we have found it in the course of measles and other epidemics.

Case II is unusually tragic, as this child apparently died from an infection picked up at a clinic designed to prevent death from other diseases, when in fact death from this type of sudden, unexpected and apparently non-specific disease is now more common than from the specific intious diseases.

These cases are presented with no attempt to base a general conclusion on them. They describe children dying apparently during their first infection, and when a relatively severe infection has been thrust upon them. In several instances there was previous passage of the infection through their own family.

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Meeting
April 18, 1959

MEETING AT CHAILEY HERITAGE (CRAFT SCHOOL AND HOSPITAL), NORTH CHAILEY, SUSSEX

AN Address was given by the President of the Section.

Many cases were shown on the wards and in other departments, to illustrate problems in rehabilitation of children with poliomyelitis, the need for team-work in the habilitation of children with developmental or multiple disabilities, and the stages of management of the programme through the full age range of childhood, including the complexities in spina bifida.

The following short papers were read:

The Study of Function and Objectives in Severely Disabled Children.—Dr. E. P. QUIBELL.

Discussion on Developmental Scales in the Functional Assessment of Handicapped Children.—Dr. ELIZABETH WHATLEY and Miss ELSPETH STEPHEN.

Review of Limb Surgery at Chailey.—Mr. W. D. COLTART.

Meeting
May 22, 1959

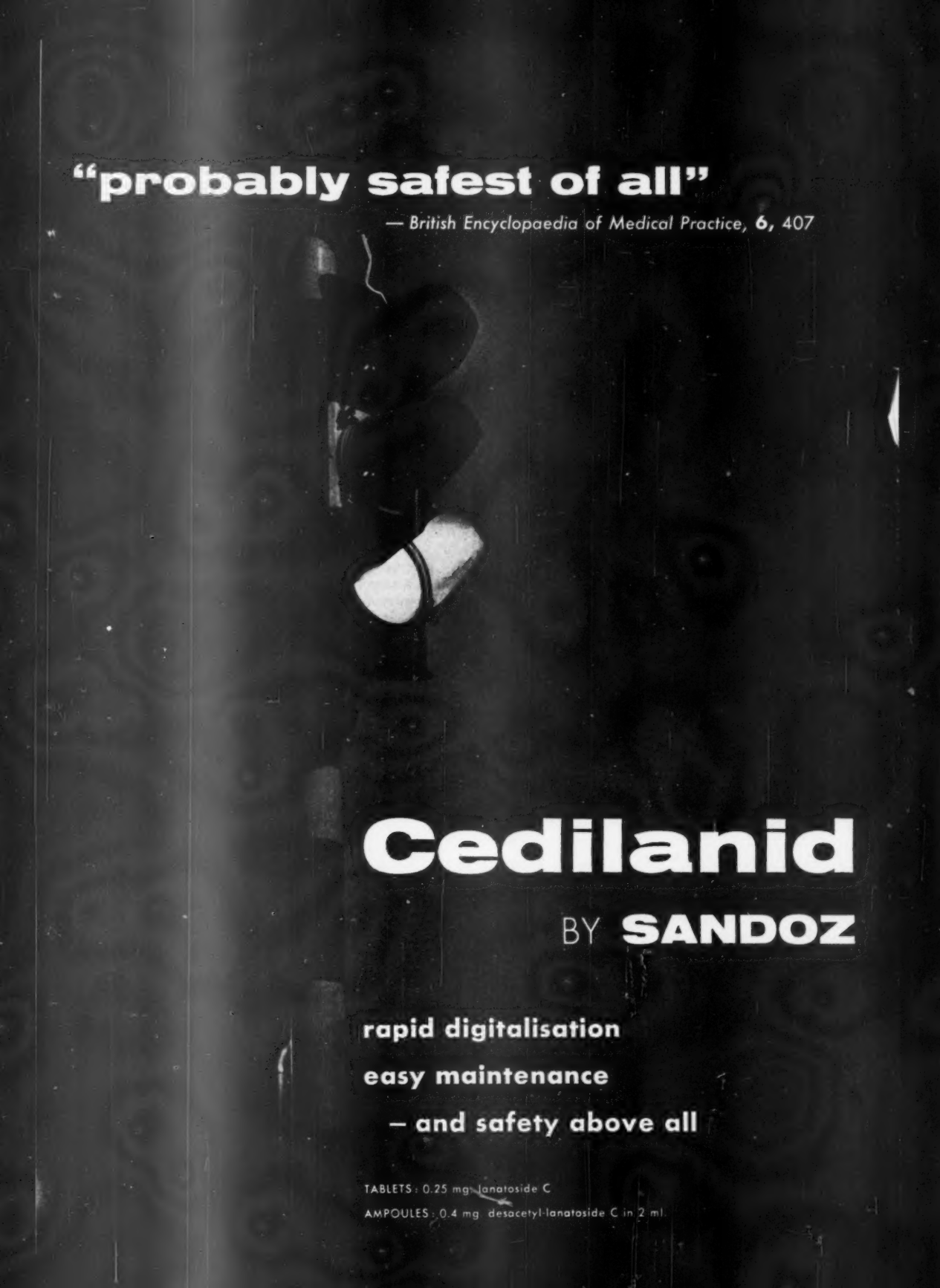
A DISCUSSION on **The Problems of Irradiation in Childhood** was introduced by Professor DOUGLAS HUBBLE; other contributions to the Discussion were as follows:

Comparison of the X-ray Histories of Healthy Children and Children who Develop Malignant Disease.—Dr. ALICE STEWART.

Radio-isotopes and Their Hazards.—Professor G. M. WILSON.

Genetic Hazards of Radiation.—Dr. C. CARTER.

A short report of this meeting appeared in the *Lancet* (1959) i, 1129.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— British Encyclopaedia of Medical Practice, 6, 407
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BOOK REVIEWS

Viral and Rickettsial Infections of Man. Edited by Thomas M. Rivers, M.D., and Frank L. Horsfall, Jr., M.D. 3rd ed. (Pp. xviii+967; illustrated. £3 3s.) London: Pitman Medical Publishing Co. Ltd. 1959.

The third edition of this now famous book compares favourably with previous editions but inevitably it has become larger and more expensive. The arrangement of material on individual virus diseases remains as before. The note on history and the adequate clinical description together with the information on epidemiology, control and the virus make this a most useful book. Detailed technical information is available for those with a special interest in virology.

The mechanism of the growth of virus and the infected cell has recently assumed great prominence. This has resulted in the introduction of three new important chapters on the Biochemistry of the Virus-Infected Cell, Virus-Host Cell Relations, and Chemotherapy in Virus Infections. On the other hand, the chapter on the use of the chick embryo has shrunk proportionately to the interest in the subject. Poliomyelitis has received more than adequate attention and is now discussed more in relation to its properties as an enterovirus, with Coxsackie and the newly recognized ECHO viruses. Mention is made of the possible role of the two latter groups as causes of paralysis alone or in association with polioviruses. Respiratory virus infections, with a new chapter on adenoviruses, are brought nearly up to date, just missing the new group of respiratory viruses. As encephalitis is now recognized to be a relatively infrequent occurrence in infection with the former so-called encephalitis viruses they are discussed under the heading of arthropod-borne virus infections together with yellow fever, dengue, &c.

There are many good plates and tables and a liberal list of references to original papers.

Immunity and Virus Infection. Edited by Victor A. Najjar, M.D. (Pp. viii+262; illustrated. 84s.) New York: John Wiley & Sons, Inc. London: Chapman & Hall, Limited. 1959.

This excellent book consists of papers presented at a symposium arranged at Vanderbilt University while F. M. Burnet was there as visiting Flexner Professor in May 1958. Only a small proportion of the contents refer to unpublished work but the authors have integrated the latest information on each subject into concise reviews of the present position in each field in such a way as to provide a very broad cover of immunity, useful for clinician and research worker. The first part of the book is on aspects of immunology, introduced by chapters by Burnet and Haurowitz, biologist and chemist respectively, who present two conflicting schools of thought on mechanism of antibody production. Other chapters discuss the delayed hypersensitive state (Pappenheimer); immunology of tissue transplantation (Owen) and immunological tolerance to living cells (Billingham); and the properdin system (Wedgwood) which it is concluded has no demonstrably significant *in vivo* role. One of the most provocative chapters is by Najjar and Robinson on their unified concept in immunological reactions which is also considered by Franklin and his colleagues in the light of their findings on high-molecular-weight gamma globulins and their complexes in rheumatoid arthritis. There are two other chapters on physicochemical studies of antibodies which are of more interest to the laboratory worker than the physician. Several chapters on bacteriophage and properties of plant and animal viruses lead into three final excellent chapters by Sabin, Paul and his colleagues, and Fox on the results of their studies with live attenuated poliovirus vaccines.

A Synopsis of Skin Diseases. By Bethel E. R. Solomons, Jun., M.A., M.D., F.R.C.P.I. (Pp. 293; illustrated. 30s.) Bristol: John Wright & Sons Ltd. 1959.

This small work is designed for the busy practitioner, for those who have to revise the subject rapidly and for the student about to take his final examination. There is no doubt that it will fill a need in this respect.

The book is packed with information on a vast number of diseases; brief mention is made of many extreme rarities and fuller accounts are given of the more common skin complaints. It will be a surprise to many general practitioners and final year students that so many skin disorders exist.

It is unfortunate that photographs cannot be included in a work of this nature because good photographs can make dermatological conditions much easier to recognize. The few illustrations which are included are pen and ink sketches of the histology of normal skin and the distribution on the body of the common skin disorders.

There is a good index and an appendix which gives a very full list of substances which may be required for patch testing in contact dermatitis and the strengths recommended for use. This appendix will be of more use to the dermatologist than to the people for whom the book was designed.

Dr. Solomons is to be congratulated on compressing so much material into a small space.

Bacterial and Mycotic Infections of Man. Edited by René J. Dubos, Ph.D. 3rd ed. (Pp. xii + 820; illustrated. £3 3s.) London: Pitman Medical Publishing Co., Ltd. 1958.

This is the third edition in eleven years of this book, the last being in 1952. It retains the general structure of its predecessors, but the text has been almost completely rewritten. Dr. Rene Dubos remains the Editor although many of the contributors are new; with two exceptions all of them work in the United States of America or in Canada.

Opening with a historical review by Professor E. G. D. Murray, in the second chapter the Editor presents his views of the evolution and ecology of microbial diseases. Subsequent chapters are more factual and deal with the general properties of bacteria and the response of the host to infection. Approximately half the book is taken up with a consideration of individual bacteria and fungi and the diseases with which they are associated. The last section includes chapters on sterilization, chemotherapy, the principles of epidemiology and diagnostic medical bacteriology. The short appendix, in which cultural methods are reviewed and a simple guide to the recognition of bacteria is provided, might with advantage be lengthened, or alternatively omitted altogether.

As a standard textbook of bacteriology this new edition can be recommended with confidence.

Treatment of Diabetes Mellitus. By Elliot P. Joslin, Howard F. Root, Priscilla White and Alexander Marble. 10th ed. (Pp. 798; illustrated. £6 2s. 6d.) London: Henry Kimpton. 1959.

It is six years since the appearance of the last edition. The new tenth edition will be welcomed as the book which is the accepted teacher and critic of what is new and a reference book of all the past. Everything new of any importance receives attention but, as Joslin says in the preface, "Recent methods have not led us to discard the old, but have made the old more practical and less costly". Joslin feels that more should be done to reduce expense and that, while taking account of stock yearly may suffice in business, diabetic adults should be checked every three months and children every four weeks. This ideal is difficult to achieve in large clinics caring for thousands of diabetics with too often the minimum of staff.

Two new aspects are recorded in this edition; first, and most important, the oral treatment with sulphonyl-ureas—mostly tolbutamide—with over 3,000 patients so treated. The experience, much the same as in other clinics, is neatly summed up in the preface, and the effect has been, for the patients, "the need for closer adherence to the diet and an added respect for insulin" and, for the doctor, the opening of many new pathways of research.

The second novelty is the acceptance as an entity of a new "lipoatrophic diabetes", first described by R. D. Lawrence in 1946. Since then a total of 9 similar cases has established it as a true separate entity, so rare as not to be of great therapeutic importance, but physiologically so strange as to provide important clues in the pathogenesis and symptomatology of diabetes mellitus.

Aged 90+, E. P. J. still preaches with a "missionary zeal" that the diabetic and his doctor should be made to realize that it is worth the effort to control the disease, as shown by a sugar-free urine, normal blood-sugar and cholesterol.

Pain. By Harold G. Wolff, M.D., and Stewart Wolf, M.D. 2nd ed. (Pp. x + 121; illustrated. 32s. 6d.) Oxford: Blackwell Scientific Publications. 1958.

There are few books which appeal to all members of the medical profession engaged in clinical work, but this is one of them. It is of course already well known and the second edition can do no more than enhance its already considerable reputation.

Discussion of the anatomy and physiology of pain forms the first chapter, and pain arising from various bodily structures the second, these two taking up three-quarters of the text. They are extremely well done and of abounding interest and information.

The last chapter on the diagnosis and management of painful conditions is too short to allow more than the annunciation of principles, albeit unexceptionable ones, and does not supply details of treatment.

The illustrations are uniformly helpful and an extensive bibliography adds considerably to the value of this already valuable book.

Psychosomatic Methods in Painless Childbirth. By L. Chertok. Translated from the 2nd French edition by Denis Leigh, M.D. (Pp. xvi + 260. 35s.) London: Pergamon Press Ltd. 1959.

When the history of obstetrics in the twentieth century comes to be written, there is no doubt that the contribution of Grantly Dick-Read and of others who have helped to develop the methods of conduct of labour known variously as "Natural Childbirth", "Childbirth without Fear" and the "Psychoprophylactic Method" will be considered to be outstanding. This book is a translation of the second edition of Chertok's original French. Though it deals mainly with the psychoprophy-

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1: Int. Congress on Rheumatic Diseases, Toronto, June 28, 1957.
2: *Lancet*, 1: 718, 1959.
3: *J. Amer. Med. Ass.*, 167: 8: 959-964 (June 21), 1958.
4: *Allergy*, 28: 97, 1957.
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lactic method developed in the Soviet Union and in France, the historical aspects of the subject are not neglected.

The book begins with a survey of early and more recent applications of hypnosis in childbirth. It goes on to a well-balanced and detailed account of the late Grantly Dick-Read's views, with the repercussions that his views had in many parts of the world.

The main thesis is a description of the psychosomatic method developed in the Soviet Union, based on Pavlov's work on conditioned reflexes. The application of this psychosomatic or psychoprophylactic method in other centres, notably in France, is also dealt with in considerable detail. The book ends with a comparison of Dick-Read's method with that evolved by the Russians and by Lamaze in France. The problems involved in these methods are thoroughly discussed. In conclusion, the author has no doubt that these methods are now generally accepted as of value. The problem is which is the best method and how is it best applied in practical obstetrics.

Dr. Leigh's translation, which cannot have been an easy task, is most successful. The book is not altogether easy to read as it has if anything attempted too wide a survey in too small a compass and the number of references and the expression of many different views makes for confusion in the reader's mind. Nevertheless this is an important study which must be read by all practising obstetrics. These methods are an integral part of modern obstetric practice.

Intra Vascular Catheterization. Edited by Henry A. Zimmerman, M.D., B.S. (Pp. xviii + 782; illustrated. £6 6s.) Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1959.

This book describes the technique of cardiac catheterization, and recounts the information that may be gathered from this procedure in relation to changes taking place in the human circulation as the result of disease.

As many as 23 authors contribute to the subject. This has inevitably meant a good deal of repetition of certain facts, and occasionally a diversity of opinions in regard to them; in a science which is so young, such overlapping is not necessarily a bad thing. Although the test is described chiefly in relation to the investigation of congenital or acquired heart disease, localized segments of the circulation also receive attention. Thus, chapters have been allocated to the pulmonary, hepatic, renal and cerebral circulation.

This book will prove a useful work of reference in any laboratory whose duties include the investigation of these separate portions of the circulation. Its ownership by those individuals concerned with the more general problems of cardiovascular disease including its diagnosis and treatment is prohibited by its high price. Nor should its possession be so coveted, in that at present this method of investigation needs to be restricted in its use since it is restricted in its usefulness. In individual cases the test has proved its worth and is necessary. It should, however, be applied only in the investigation of a patient in whom the diagnosis of a cardiovascular fault will not yield to simpler measures, and when it is certain that it will provide information greater than these. Its risks, the great expense connected with its employment, and the discomfort which it entails to a patient already incapacitated by an illness, should be an insurance against adopting it as a routine procedure. It should always fulfil a need, and never be deemed an adventure.

The Life and Times of Sir Charles Hastings. By William H. McMenemey, M.A., D.M., F.R.C.P., D.P.M. (Pp. xii + 516; illustrated. 50s.) Edinburgh and London: E. & S. Livingstone Ltd. 1959.

This is a remarkably interesting and informative book giving clear evidence of wide research into contemporary literature. It contains a full-scale biography of Sir Charles Hastings, a very detailed (perhaps too detailed) account of the origin of the Provincial Medical and Surgical Association and its conversion into the British Medical Association, a good though necessarily incomplete summary of the events which led up to the passing of the 1858 Medical Act, and many excellent pen-pictures of medical life in the first half of the Victorian era. The author has had access to several unique sources which have enabled him to provide accurate and authentic information. The book will in future be an indispensable historical source for that period of the development of medicine in this country.

The style of writing is leisurely and natural, and the author lightens up bare facts with witty comments, interesting allusions, and gentle irony, so that the interest seldom flags.

The careful reading of this book leaves the impression that Sir Charles Hastings was a much more able man than is sometimes thought; he was not only one of the most gifted physicians of his generation but he grasped the essentials necessary for medical union, and by his tenacity of purpose, his genius for administration and his powerful advocacy founded a great Association and greatly advanced the status of the whole medical profession.

Dr. McMenemey has made a major contribution to the medical history of the middle of the nineteenth century.

Allgemeine Pathologie. By Dr. Erich Letterer. (Pp. xx+849; illustrated. DM 69) Stuttgart: Georg Thieme Verlag. 1959.

Two features have distinguished the treatment of "General Pathology" by German authors from that by British writers on this subject: first, their preoccupation with the cell as the focal point for study—a legacy of Virchow; and second, their lesser attention to problems of ætiology whose solution has contributed so greatly to the growth of preventive and occupational medicine. It may prove, however, that during the next era of progress in pathology this concentration on pathological cytology may bring greater rewards than in the past. For as pathologists and epidemiologists have established control over most of the important parasitic diseases and must henceforth transfer their attention more and more to the problems of neoplasia, the pathology of the cell rather than that of the tissue or organ will figure with increasing prominence in their researches.

This volume is in the best traditions of German pathology. Professor Letterer's exposition of the subject has a freshness and continuity rarely to be found except in first editions, and he has taken the opportunity to graft the rapidly expanding discoveries of modern biophysical and biochemical cytology on to knowledge acquired through older and more established work. Pathologists in the English-speaking countries would benefit from the study of these trends of thought as exemplified in this and other recent German expositions of the general principles of their subject. The time may be near when the outlook in general pathology in this country might undergo a similar re-orientation with profit, and a closer association be sought with modern cytology and its new and powerful techniques.

The volume is beautifully produced and magnificently illustrated with some six hundred photographs and diagrams. It is documented adequately, especially as regards Continental authors, but as a book it is intended rather for continuous reading than for reference.

Cold Injury, Ground Type. Medical Department, United States Army. Editors: Col. John Boyd Coates, Jr., M.C., and Elizabeth M. McFetridge, M.A. (Pp. xxi+570; illustrated. $6.25). Washington, D.C.: Office of the Surgeon General, Dept. of the Army. 1958.

Never can one disease have been subjected to a review so painstaking, detailed and well documented as this. It is not the sort of book to which doctors are accustomed: as might be expected of an official book, it is officially arranged. But no doctor attached to the armed service or to an amateur expedition to high altitudes or latitudes can afford to miss it.

The whole pathology of cryopathy is here, but little has been added in recent years. Of more importance is the practical advice. The knowledge of how to avoid cold injury was available before the U.S.A. entered World War II. In the words of General Hays, "there are no absolute excuses for the epidemics of cold injury which occurred on the Continent of Europe during World War II" . . . there was "failure to learn the lessons of the past". In particular English experience gained in World War I, in the Himalayas and on polar expeditions, was neglected.

In consequence, in the first winter after D-day there were 45,000 casualties from cold injury in Europe in the army of the U.S.A. The British suffered 206. In Italy during 1943–4, the British casualties from this cause were 102, the American 4,560. The explanations were boots, socks, and, most important of all, discipline.

But the Americans learned their lesson, even though they learned it late. The basis of their final instructions was admittedly an article in the *Practitioner* of January 1942, itself a digest of a memorandum submitted by invitation of the War Office in 1940. The total number of admissions for cold injury in the U.S. Army in the period 1942–45 was 82,580. The Surgeon-General is obviously determined that this shall not happen again.

Postural Drainage and Respiratory Control. By E. Winifred Thacker, M.C.S.P. 2nd ed. (Pp. ix+62; illustrated. 10s. 6d.) London: Lloyd-Luke (Medical Books) Ltd. 1959.

This small book has, in the course of three years, reached a second edition. The present edition illustrates the technique of postural drainage and gives the various positions in which the patient should be placed so that gravity can assist in the drainage of the bronchi. Moreover, a few changes have been made since the first edition, making it very practical from the point of view of continuation of treatment outside hospital. The small section on tipping in the home is of considerable practical value.

The book illustrates the importance of the determined enthusiasm, not only on the part of the physiotherapist, but also on the part of the patient himself who must, of course, have a full understanding of the significance of his treatment to enable him to co-operate.

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